

Bland, J. D. P., Weller, P. & Rudolfer, S. (2011). Questionnaire tools for the diagnosis of carpal tunnel syndrome from the patient history. *Muscle & Nerve*, 44(5), pp. 757-762. doi: 10.1002/mus.22158



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**Original citation:** Bland, J. D. P., Weller, P. & Rudolfer, S. (2011). Questionnaire tools for the diagnosis of carpal tunnel syndrome from the patient history. *Muscle & Nerve*, 44(5), pp. 757-762. doi: 10.1002/mus.22158

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## **Questionnaire tools for the diagnosis of carpal tunnel syndrome from the patient history**

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Running title – Questionnaire diagnosis of CTS

Word count - Abstract 178, Main Article – 3257 excluding references

## ABSTRACT

### INTRODUCTION

There remains no ‘gold standard’ for the diagnosis of carpal tunnel syndrome (CTS). Clinical diagnosis is often held to be paramount but depends on the skills of the individual practitioner. This paper describes two mathematical approaches to the analysis of a history obtained from the patient by questionnaire.

### METHODS

We used two previously published instruments and two new ones, one conventional logistic regression analysis and one artificial neural network, to analyse data from a population of 5860 patients referred for diagnosis of hand symptoms and evaluated their ability to predict whether nerve conduction studies would confirm the diagnosis of CTS using receiver operating characteristic curves

### RESULTS

Both of the new instruments performed better than the existing tools achieving sensitivity of 88% and specificity of 50% in predicting abnormal median nerve conduction at the carpal tunnel. When combined 96% sensitivity and 50% specificity were achieved

### DISCUSSION

The combined instrument performs well enough to be used as a preliminary screening tool for CTS, for self-diagnosis by the patient and as a supplement to diagnosis in primary care.

### **Keywords**

Carpal tunnel syndrome

Diagnosis

Questionnaire

Neural Networks

Nerve Conduction Studies

## INTRODUCTION

Although there is general agreement about what clinical features are indicative of CTS, there is no internationally agreed definition and though it is easy to recognise a typical case clinically there are many patients with atypical symptoms, some of whom may benefit from treatment. The definitive treatment is surgical decompression, a procedure which is mostly very successful, but which results in a small incidence of significant morbidity. It is thus important that patients who could benefit from surgery are identified as accurately as possible.

Several attempts have been made at formalising diagnostic criteria for CTS. Some are simply the opinion of an expert in the field, creating a definition for the purposes of a particular study. Clinically definite CTS in one Scandinavian study was defined as “Recurring night-time or activity related numbness or tingling involving the palmar aspects of at least two radial fingers”<sup>1</sup>. A definition for use in epidemiological studies and occupational health surveillance was proposed in 1998 – “A clinical syndrome caused by compression of the median nerve as it passes through the carpal tunnel: Surveillance criteria - Pain or paraesthesia, or sensory loss in the median nerve distribution and one of: Tinel's test positive, Phalen's test positive, nocturnal exacerbation of symptoms, motor loss with wasting of abductor pollicis brevis, and abnormal conduction time.”<sup>2</sup> This makes it explicit that CTS is a condition which results from a particular pathological process at a specified site, and it allows the inclusion of a laboratory measurement (NCS) as a supplementary diagnostic criterion. These diagnostic criteria are not intended for making treatment decisions in the individual patient and err on the side of inclusivity rather than diagnostic specificity. No single clinical feature, such as Phalen’s sign, is sufficient to make the diagnosis, and the syndrome cannot be defined solely by a laboratory measurement such as NCS.

An alternative to expert opinion is provided by mathematical approaches based upon the study of the degree of association between clinical features and diagnosis. For any clinical feature which is either present or absent the association with the diagnosis can be expressed as sensitivity and specificity, or positive and negative predictive values. Clinical diagnosis however depends on the synthesis of many items of information about the patient and mathematical methods also exist for this.

Logistic regression is a statistical technique, widely used in the health sciences,<sup>3,4</sup> for estimating the probability of a disease being present in a patient, based on the values of several covariates. In order to convert the probability of a disease to a diagnosis, the simplest approach is to use a cutpoint,  $c$ : if the probability of the disease is at most  $c$ , then the diagnosis based on the logistic model is “disease absent”; otherwise, the diagnosis is “disease present”. Failing any evidence to the contrary, the usual value of  $c$  is 0.5. Estimation of the logistic regression model requires iterative statistical methods, since the equations involved do not have an exact solution. The simplest method of evaluating the performance of the logistic regression model is to split the dataset (if sufficiently large), containing the values of the covariates and the “true” diagnosis, into two similar but disjoint training and test subsets, fitting the model to the training subset and testing it on the test subset.

Artificial neural networks (ANNs) are classifier systems, based on simplified models of the cerebral system, that have been applied to a number of clinical applications.<sup>5</sup> The basic ANN processing unit is a node which operates in a similar way to the biological neuron. A number of nodes are combined in interconnected layers to process information. Importantly ANNs can be trained to classify data for a specific task. The popular method, applied in this work, is to construct two independent datasets containing a matched set of inputs and outputs. Through repeated presentation of the first dataset the ANN internal parameters are gradually adjusted to minimise the error between obtained and expected outputs. When this stage is complete the second dataset tests the ability of the trained ANN to classify unknown data. If this result is acceptable the ANN can be used to classify new cases.

The use of clinical questionnaires in CTS is not new. One of the earliest and most widely used examples is the CTS severity instrument devised as a measure of subjective symptom severity and functional impairment by Levine et al in 1993.<sup>6</sup> Attempts have been made to use this for diagnostic purposes, with limited success.<sup>7,8 9</sup> Other similar tools have not gained such widespread acceptance.<sup>10-12</sup> The earliest formal tool designed to aid diagnosis is the Katz hand diagram.<sup>13</sup> We have previously published an instrument which combines 8 variables which can be obtained from the patient without any intervention from a clinical professional to provide an overall

probability of CTS.<sup>14</sup> One other diagnostic questionnaire based purely on data derived from the patient history has been proposed<sup>15</sup> and three which include data derived from physical examination, the CTS-7 instrument from Ontario.<sup>16</sup> and two un-named tools.<sup>17,18</sup>

In the absence of any ‘gold standard’ with which to compare, it is impossible to measure the performance of a prototype tool with complete accuracy and in order to create a logistic regression model or an ANN one has to make an arbitrary choice of how to divide the population of patients used to calculate the coefficients into CTS and non-CTS cases. Three existing tools<sup>14-16</sup> demonstrate different approaches.

Our own earlier model defined cases for model generation only by the results of nerve conduction studies and is therefore optimised to predict whether the NCS will be abnormal rather than whether the patient has CTS. This instrument achieves 76% sensitivity and 70% specificity in predicting abnormal NCS. A modified version of this has been used in Glasgow where it achieved 82% sensitivity and 67% specificity.<sup>19</sup> A Brazilian regression model achieved 67% sensitivity and 69% specificity.<sup>17</sup>

Kamath and Stothard<sup>15</sup> used the clinical response to surgical decompression as the marker for CTS, patients reporting a good response to surgery 2 weeks after operation being assumed to have CTS. The method used to arrive at the questions included in the questionnaire and their weightings is not explicit. This instrument was reported to achieve 85% sensitivity, compared with 92% for NCS, in predicting a successful outcome for surgery. No data is available for diagnostic specificity. The use of surgical outcome as a proxy for the diagnosis is appealing as the decision to be made is primarily whether to operate and anything which accurately predicts the response to surgery would be very useful. However, as a gold standard for diagnosis, surgical response has some shortcomings. Other disorders may improve symptomatically in response to surgery and the associated rest and recovery period and failure to respond to surgery does not necessarily indicate that the original problem was not CTS.

The clinical features used in the CTS-7 were compiled through a Delphi consensus development process by a group of ‘CTS-experts’ and a logistic regression model

derived using a set of fictitious clinical vignettes including all of the features which had featured in the original list from the Delphi exercise in roughly equal proportions and every possible combination. Each vignette was classified as representative of CTS or not by a second, independent, panel of experts. This tool was thus created and weighted without reference to any patient population, both development and validation being against expert opinion.

We report here an updated version of our original diagnostic tool using traditional regression methods and also used an artificial neural network system with the same input data as an example of an alternative computational approach.

## METHODS

The Canterbury Carpal Tunnel Database contains computerised clinical data on almost all patients presenting to medical attention with suspected carpal tunnel syndrome in a geographical area with a population of 700,000 people. All clinicians dealing with the problem are encouraged to refer every patient in whom the diagnosis is considered for nerve conduction studies with the intent that all patients should be captured and tested. As a result of this inclusive policy, nerve conduction studies are performed on a substantial number of patients who do not in fact have CTS and the database consists of approximately 60% patients with abnormal NCS consistent with CTS and 40% patients without such results. Although these two patient groups will include both false negative and false positive NCS tests it is likely that the majority of patients in the NCS-positive group do have CTS and the majority in the NCS-negative group do not.

We abstracted anonymised patient data collected during the period 2000-2007 from 5280 subjects, and divided this into subsets to be used for model generation and testing. Most of the data required to complete the Kamath questionnaire and the CTS-7 instrument is also stored in the database but we did not routinely record the presence of symptoms during a previous pregnancy or neck pain in the core data set so these were added prospectively for a further cohort of patients to allow evaluation of the performance of the Kamath tool in this population. The CTS-7 includes examination findings (Tinel's and/or Phalen's signs) and we wished to study data which could be

collected from the patient without medical intervention. Only patients making their first presentation with possible CTS were included, excluding those with previous surgery to either side or recurrence after successful conservative treatment. We did not exclude patients with concomitant pathologies such as diabetic polyneuropathy or ulnar neuropathy as we wished the results to be as generalisable as possible to normal practice.

The same model generation dataset was presented to both the neural network software (NeuralWorks Professional, Neuralware, Pennsylvania) and to a logistic regression analysis system (Stata, StataCorp LP, Texas). In the model generation dataset, cases were defined as ‘CTS’ if the nerve conduction results were abnormal suggestive of CTS in either or both hands and as ‘not-CTS’ if both hands had normal NCS. The resulting models were then applied to new data from the test set to measure their performance in predicting CTS or not-CTS.

Nerve conduction studies were carried out on both hands of all patients to AANEM standards.

## RESULTS

All of the methods proved able to classify new cases as CTS or Non-CTS with a performance better than chance. An overall comparison of their performance is shown in figure 1 as receiver operating characteristic curves from which it can be seen that the artificial neural network and logistic regression are virtually indistinguishable from each other, and better than the previous logistic regression, which in turn is better than the Kamath score. Both our neural network and regression models are built using an inclusive policy involving 125 variables which provides every piece of clinical information available to the model for decision making. We did not employ methods for simplifying the regression model because we wanted to maintain close comparability with the neural network. Features with the largest positive and negative weightings are shown in table 1. In order to express the performance of these tools in terms of sensitivity and specificity one has to choose one point on the ROC curve as a cut-off value and it is conventional to optimise this choice for overall accuracy as the point at the greatest perpendicular distance from the diagonal line which represents a



test with no discriminating ability. For our models this point falls at a score of 0.55 for the artificial neural network and 0.63 for the regression model. The exact value used for a cutoff will depend to some extent on clinical circumstances. When screening for possible cases a lower cut-point would trade off some specificity in return for greater sensitivity while for identifying clinically certain cases for a trial a higher cut-point yields only patients with highly probable CTS but excludes more clinically atypical cases. Using values optimised for overall accuracy the sensitivity and specificity of the two approaches are shown in table 2. Finally, as each model identifies a slightly different subset of patients as having CTS, we looked at the combined performance obtained if a patient was classified using the output of both models, classifying as CTS if either or both models predicted CTS and as non-CTS only if both models predict non-CTS. The sensitivity and specificity of this combined approach are shown in table 3.

## DISCUSSION

There are points of similarity and dissimilarity between the two mathematical methods, as would be expected from distinct approaches to the diagnostic problem. Table 2 gives the ten most positive and ten most negative network weights and regression standardised weights. Examining this table leads to some interesting observations regarding the clinical picture, aetiology and epidemiology of CTS. The network and regression have three variables out of the top ten positive variables in common for predicting CTS, and seven out of the top ten negative variables for predicting non-CTS. There is agreement on greater age being the most predictive of CTS, also middle and ring finger distribution of symptoms and years since retirement increase the chance of CTS. The network includes five Boston variables among the top ten in favour of CTS, while the regression has none. Conversely, ex-smoker or lifelong non-smoker status is predictive of CTS in the regression model but not in the network. The appearance of smoking status in the regression model is somewhat unexpected, with lifelong non-smokers apparently being more likely to have CTS than ex-smokers who in turn seem to have a higher risk than current smokers. This is directly contrary to the findings of two previous epidemiological studies of risk factors for CTS.<sup>20,21</sup> Of the seven common variables predicting non-CTS, Vibration white finger, Boston weakness on the right, and hours of keyboard activity have the

same ranking in the two models. Typically ulnar nerve distribution of symptoms, and height occupy the bottom two places in the list of negative weights against CTS, but in different orders for the two models. Occupational keyboard use making CTS less likely is contrary to much popular and occupational health perceived wisdom but is in agreement with two of the better recent studies of the issue.<sup>22,23</sup> The differences between the two models may reflect the fact that most of the variables have only a small predictive value individually and the generation process for the neural network in particular includes some random elements so that, given a set of many roughly similar variables to choose from, a different set may be selected each time a network is trained. The presence of age as the strongest predictive factor in both models should remind us that CTS, frequently described as a disorder predominantly of middle aged women, is in fact very common in the elderly and frequently misdiagnosed.

The regression model has selected more of the variables which would be familiar to the average clinician as markers of carpal tunnel syndrome – diurnal variation in symptoms, anatomical distribution of paraesthesiae, obesity, the last of these being striking in that, in the neural network model, the variable body mass index (BMI) which is dependent on height and weight, appears as a positive predictor while weight itself appears as a negative predictor. In the regression model this situation is reversed with weight appearing as a positive predictor and BMI as a negative one.

We reviewed the case histories of a sample of patients who were mis-classified by both analytic methods. In the case of patients classified by the models as CTS who actually had normal nerve conduction studies it seemed likely that many of these were examples of false negative nerve conduction studies. 24/62 of these patients were evaluated by an experienced clinician (JDPB) as highly probable CTS on the evidence available at the time of assessment. Other recognisable groups of patients often misclassified by the models as CTS included those with ulnar nerve lesions at the elbow and patients with rheumatological disorders. The patients mis-classified as normal but having abnormal nerve conduction studies suggestive of CTS were much more heterogeneous but some of these patients clearly had dual pathology with the second condition dominating the clinical picture and in those with only neurophysiological evidence of CTS the clinical histories were often obviously atypical on review.

Despite our best efforts at including every possible clinical feature of the patient history which experienced clinicians use to make the diagnosis of CTS and the most sophisticated analysis tools available, it appears that none of these instruments achieve perfect prediction of NCS findings consistent with CTS. Why is this? Firstly we know that NCS will not always be right. Normality of nerve conduction studies is defined statistically in such a way that there will be a false positive rate, the magnitude of which is arbitrarily set by the cut-off values chosen. One would hope that a diagnostic tool would return the clinically 'correct' answer in asymptomatic individuals with NCS measurements which just happen to lie outside the limits which have been set for normality, be that 2.5 standard deviations from a mean value, or 99<sup>th</sup> percentile. Disagreement between diagnostic instrument and NCS on these grounds is inevitable. Secondly we believe that NCS have a false negative rate but have no way of knowing what it is. Studies where clinical diagnosis is used as the gold standard for comparison give estimates ranging from 2-30%. Taking a successful outcome of surgery as a marker for the diagnosis suggests that the false negative rate is of the order of 5%. Whatever the actual figure, it is clear that these cases also should produce disagreement between a perfect clinical instrument and the neurophysiological diagnosis. A less considered issue is that of the accuracy of clinical diagnosis. A clinician's opinion is often held up as the definitive arbiter of whether a patient has CTS or not and, curiously, in this field this is rarely questioned. However, clinical diagnosis in other fields is manifestly not 100% accurate for many common disorders and there is no reason to believe that it is reliable for CTS. There are ample studies of failed treatment showing that initial diagnoses of CTS were incorrect, it subsequently becoming apparent that the patients had polyneuropathy, ulnar nerve lesions, cervical radiculopathy, rheumatological disorders, multiple sclerosis, syringomyelia or motor neurone disease.<sup>24</sup> The 39% failure rate of surgery in Canterbury patients with normal NCS suggests that at least here, some patients get as far as surgery without the real cause of their symptoms having been established. If clinical diagnosis itself is not perfect then our diagnostic instruments, which are based upon the same input data, are also likely to be imperfect. There is no immediate prospect of a definitive diagnostic test becoming available which will allow both absolutely accurate diagnosis and the full evaluation of the performance of these other methods. However, the best units achieve success rates in treating CTS in excess of

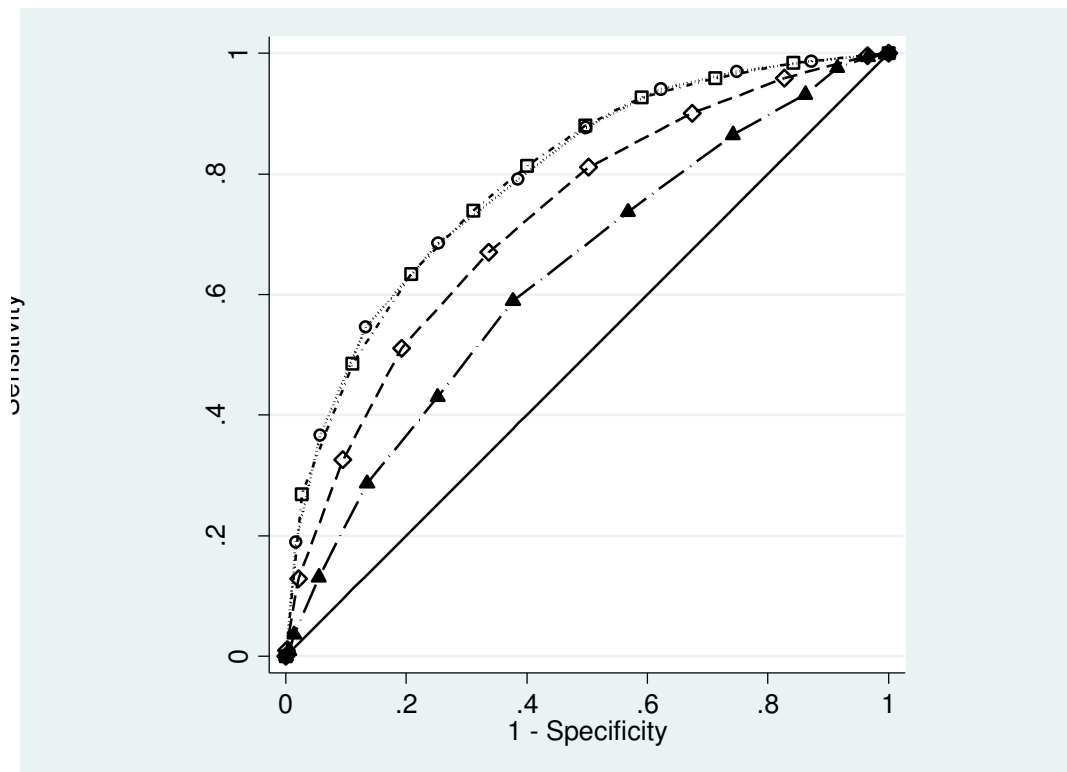
98% patient satisfaction, probably through a combination of good patient selection and expert treatment. The use of formal tools may help less experienced clinicians to emulate this.

The full questionnaire is too lengthy to include in a published paper and the mathematical models used to evaluate the answers are too complex for simple scoring on paper. We are therefore intending to make the entire questionnaire available online at [www.carpal-tunnel.net](http://www.carpal-tunnel.net) - a non-commercial site created to host this tool.

FIGURE CAPTION

Figure 1

Receiver operating characteristic curves for the four different diagnostic tools evaluated, Kamath score (solid triangles, area under curve 0.63), original regression model (open diamonds, area under curve 0.73), current regression model (open squares, area under curve 0.79), artificial neural network (open circles, area under curve 0.79)



Receiver operating characteristic curves for the various diagnostic tools

Key  
 ANN4 ( ···○··· ) JB LR ( - - ◆ - - )  
 Kamath Score ( —▲— ) SR LR ( ···□··· )

Table 1

**Predictors of Abnormal/Normal NCS consistent with CTS****Ten most positive predictors****Artificial Neural Network****Regression model**

<b>Variable</b>	<b>Weight</b>	<b>Variable</b>	<b>Standardised Weight, z</b>	<b>95% CI for z</b>		<b>Odds Ratio</b>	<b>95% CI for OR</b>	
Increasing age	3.23	Increasing age	9.26	7.3	11.22	1.05	1.04	1.06
Boston numbness severity - R	1.41	Symptoms worse on driving	5.26	3.3	7.22	1.72	1.41	2.11
Boston tingling severity - R	1.36	Symptoms worse first thing in morning	4.64	2.68	6.6	1.60	1.31	1.95
Body mass index	1.29	Lifelong non-smoker	4.58	2.62	6.54	1.79	1.40	2.30
No response to Diuretic	1.08	Middle and ring finger distribution	4.5	2.54	6.46	3.13	1.90	5.13
Years since retirement	1.03	Thumb, index and middle finger distribution	4.47	2.51	6.43	2.63	1.72	4.01
Boston telephone grip difficulty - L	1.01	Weight	3.32	1.36	5.28	1.09	1.03	1.14
Middle and ring finger distribution	0.97	Self reported heavy manual work	3.12	1.16	5.08	1.64	1.20	2.25
Boston night pain severity - R	0.91	Ex-smoker	2.99	1.03	4.95	1.46	1.14	1.88
Boston book holding difficulty - R	0.90	Years since retirement	2.68	0.72	4.64	1.01	1.00	1.02

**Ten most negative predictors****Artificial Neural Network****Regression Model**

<b>Variable</b>	<b>Weight</b>	<b>Variable</b>	<b>Standardised Weight</b>	<b>95% CI for z</b>		<b>Odds Ratio</b>	<b>95% CI for OR</b>	
Boston subjective weakness severity - L	-1.00	Has never tried a wrist splint	-2.47	-4.43	-0.51	0.67	0.49	0.92
Boston day pain duration - R	-1.01	Body mass index	-2.66	-4.62	-0.7	0.83	0.73	0.95
Boston grocery carrying difficulty	-1.02	Raynaud's phenomenon	-2.86	-4.82	-0.9	0.41	0.22	0.75
Employment status - full time education	-1.07	Boston day pain duration - R	-2.96	-4.92	-1	0.70	0.55	0.88
Vibration white finger	-1.11	Vibration white finger	-3.01	-4.97	-1.05	0.26	0.11	0.63
Raynaud's phenomenon	-1.17	Boston jar opening difficulty - L	-3.1	-5.06	-1.14	0.73	0.59	0.89
Boston weakness severity - R	-1.36	Boston weakness severity - R	-3.15	-5.11	-1.19	0.68	0.53	0.86
Hours of keyboard use daily	-1.57	Hours of keyboard use daily	-3.75	-5.71	-1.79	0.92	0.88	0.96
Height	-1.62	Little and ring finger distribution	-3.88	-5.84	-1.92	0.30	0.17	0.55
Little and ring finger distribution	-1.97	Height	-4.29	-6.25	-2.33	0.90	0.86	0.94

'Boston' variables are elements of the Boston/Levine CTS subjective severity assessment tool

'R' and 'L' for these variables indicate the answers given for the right and left hands separately

The Standardised Weights for the regression model are given instead of the raw weights since assessment of the statistical significance of a weight depends on the ratio of its raw value to its standard error (the Standardised Weight)

Table 2

**Classification of new cases by the two methods**

		<b>Artificial neural network</b>		
		<b>CTS</b>	<b>Normal</b>	<b>TOTAL</b>
<b>NCS result</b>	<b>CTS</b>	1397	183	1580
	<b>Normal</b>	518	518	1036
	<b>TOTAL</b>	1915	701	2616
		Sensitivity	88.4%	
		Specificity	50.0%	
		<b>Regression model</b>		
		<b>CTS</b>	<b>Normal</b>	<b>TOTAL</b>
<b>NCS result</b>	<b>CTS</b>	1127	453	1580
	<b>Normal</b>	286	750	1036
	<b>TOTAL</b>	1413	1203	2616
		Sensitivity	71.3%	
		Specificity	72.4%	

McFadden's Pseudo R-squared value for the logistic regression model is 0.2962.  
ANN confusion matrix value is 0.3022

Table 3

**Classification of new cases by combination of both models**

		Questionnaire Evaluation		TOTAL
		CTS	Normal	
NCS result	CTS	1516	64	1580
	Normal	518	518	1036
TOTAL		2034	582	2616
		Sensitivity	95.9%	
		Specificity	50.0%	



**Acronyms/Abbreviations**

CTS – Carpal Tunnel Syndrome

NCS – Nerve conduction studies

ANN – Artificial Neural Network

LR – Logistic regression

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