Prospective analysis of the accuracy of diagnosis of carpal tunnel syndrome using a web based questionnaire

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Prospective analysis of the accuracy of diagnosis of carpal tunnel syndrome using a web based questionnaire

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Contributors – Peter Weller and Stephan Rudolfer created the mathematical models used to analyse the questionnaire and performed the statistical analysis of the prospectively collected data. Jeremy Bland reported and graded all of the nerve conduction studies, and collated the questionnaire data from the website. All three authors contributed to the drafting of the paper and jointly act as guarantors.

Figures – 4

Word Count – 2671 excluding references

Keywords – Carpal Tunnel Syndrome, Diagnosis, World-wide-web, Questionnaire, Sensitivity and Specificity

ABSTRACT

Objective – To confirm the accuracy of a diagnostic questionnaire for carpal tunnel syndrome (CTS) when presented via a public website rather than on paper

Design – Prospective comparison of the probability of CTS as assessed by the web-based questionnaire at http://www.carpal-tunnel.net with the results of nerve conduction studies

Setting – Sub regional neurophysiology laboratory serving a population of 700,000 in East Kent, UK

Participants – All individuals referred for initial diagnostic testing for new presentations with suspected CTS from April 2011 to March 2013. No exclusions were made on grounds of age, gender or coincident pathology.

Main outcome measure – Nerve conduction results confirming CTS. The severity of median nerve impairment demonstrated was also assessed using a validated neurophysiological scale.

Results – The web based version of the diagnostic questionnaire was as accurate as the original paper version with an area under the receiver operating characteristic curve of 0.79. There was also a significant correlation between the diagnostic score given by the website and the severity of CTS with higher scores being associated with greater nerve dysfunction.

Conclusion – Completion of the symptom questionnaire on the website by patients at home provides a prediction of the likelihood of CTS which is sufficiently accurate to be used in initial planning of investigation and treatment.

STRENGTHS AND LIMITATIONS OF THIS STUDY

Strengths

- Prospective design
- Large numbers
- Objective confirmation of diagnosis using best available current methods
- Unselected patient population

Weaknesses

- Lack of blinding

WHAT THIS PAPER ADDS

What is already known on this subject

Self completed patient questionnaires have been used to make diagnoses with acceptable accuracy compared to conventional clinical assessments for screening purposes previously. Such tools have not been made widely available to patients on the internet

What this study adds

This study shows that a self completed diagnostic questionnaire on a public website can make the diagnosis of carpal tunnel syndrome with considerable accuracy in patients with hand symptoms. It also shows that the analysis of the questionnaire using mathematical approaches can give a diagnosis in terms of probability which can be validated against an objective test as an accurate assessment.

INTRODUCTION

The diagnosis of carpal tunnel syndrome (CTS) is often straightforward, requiring no more than listening to the patient's description of the characteristic timing and distribution of the symptoms and a focused examination of the hands to look for obvious signs. Nevertheless there remains no reliable 'gold standard' test for the diagnosis and an extensive literature exists debating the relative merits of clinical diagnosis, nerve conduction studies (NCS), imaging methods and response to treatment as elements of the definition for the syndrome. NCS and imaging produce results which can be quantified and analysed for their diagnostic properties but studies of clinical diagnosis, which are comparatively rare, generally approach it as a binary opinion – the patient either does, or does not have, CTS. This does not fairly represent the subtlety of clinical opinion which encompasses a range of certainty rather than being an absolute. Human beings however are rarely able to express their degree of certainty consistently in numerical form for analysis. We have been interested for some years in whether the answers to a questionnaire relating to the symptoms could be analysed mathematically to arrive at an estimate of the probability of CTS, based on the same information used by clinicians, but which would be reproducible and quantifiable so that it could be compared with the results of diagnostic tests.

Interest in standardized questionnaires for diagnosis is not new and some questionnaires have been shown to achieve good agreement with conventional clinical diagnosis for common conditions, for example in asthma[1] or restless legs syndrome[2] but these tools are not widely available to patients to use unaided.

An early version of our diagnostic questionnaire achieved 79% sensitivity and 55% specificity for the diagnosis of CTS when the result of nerve conduction studies was used as the reference standard.[3] We refined and extended the questionnaire and by 2011 the paper version had grown to 6 pages and improved to 96% sensitivity and 50% specificity in predicting the NCS result when tuned to optimize sensitivity in order to avoid missing treatable disease. [4] Not only was the paper questionnaire cumbersome but the mathematical methods used to analyse the answers – a logistic regression model and an artificial neural network – required the aid of a computer to calculate the probability of CTS. We therefore created a website on which patients could complete the questionnaire and which would perform the calculations immediately it was completed. Our assessments of the performance of the questionnaire however had been made using the paper version and we could not be sure that it would perform in the same way when presented in online format. This study therefore prospectively analyses the diagnostic accuracy of the web-based version of the questionnaire, again using the results of nerve conduction studies as the reference standard for CTS.

METHODS

The collection of a standardized clinical history by questionnaire has been standard practice in the Canterbury department of clinical neurophysiology for 20 years and it was not considered necessary to seek either ethical committee approval nor written patient consent for transferring this process of data collection from paper to the

website. Patients retained the option of completing the paper form of the questionnaire if they did not wish to use the web version.

Patients referred for investigation of possible carpal tunnel syndrome to the sub-regional department of clinical neurophysiology in Canterbury, Kent, UK between 1.4.2011 and 1.4.2013 were invited, in their appointment letter, to visit the website at http://www.carpal-tunnel.net prior to their appointment and to complete the questionnaire. To do this, patients had to create a user account on the website but we recommended that they create a user identity which did not reveal who they were to third party observers viewing interactions on the site. We provided them, also in the neurophysiology appointment letter, with a reference number to be entered into the site registration page which would identify them uniquely to us. The key data table linking these reference numbers to patient identities is not stored anywhere in the website but is kept in the internal computerized records of the neurophysiology department within the secure boundaries of the hospital IT systems.

On attending the neurophysiology department, patients were asked whether they had been able to complete the questionnaire on the website and those who had not been able to do so were given the original paper version to complete. All patients then had nerve conduction studies performed for CTS according to guidelines published by the American Association of Neuromuscular and Electrodiagnostic Medicine.[5] The nerve conduction results were graded using the Canterbury severity scale for CTS [6], which represents the changes in sensory and motor nerve conduction velocities and amplitudes as a numerical scale increasing in severity from 0 (no abnormality) to 6 (extremely severe CTS). No exclusions were applied on grounds of age, gender or coincident pathology.

In order to work with the patient rather than the hand as the unit of analysis each patient was classified using the nerve conduction results as either CTS, if either hand showed at least grade 1 CTS, or normal. The diagnostic scores produced by the website were then compared against the presence or absence of CTS and also, in a secondary analysis, against the neurophysiological severity of the worst hand. Finally, as 6% of patients fail to attend our clinic after completing the web questionnaire, we looked at the distribution of website diagnostic scores to see if this subpopulation differed from the patients who did attend for testing.

The web-based questionnaire does not return a binary verdict – CTS, yes or no – but a percentage probability of CTS. The sensitivity and specificity of the questionnaire can therefore be tuned to favour the detection of more disease or the exclusion of more patients who do not prove to have CTS by adjusting the score which is taken as indicating CTS. This variable diagnostic performance was calculated across the full range of scores by constructing a receiver operating characteristic curve for comparison with that derived for the paper questionnaire previously. The relationship between the web questionnaire score and the neurophysiological severity of CTS in the worst hand of patients who did have evidence of CTS was assessed using Pearson correlation. The website scores of patients who did, and did not , attend for testing were compared with non-parametric tests as the scores are

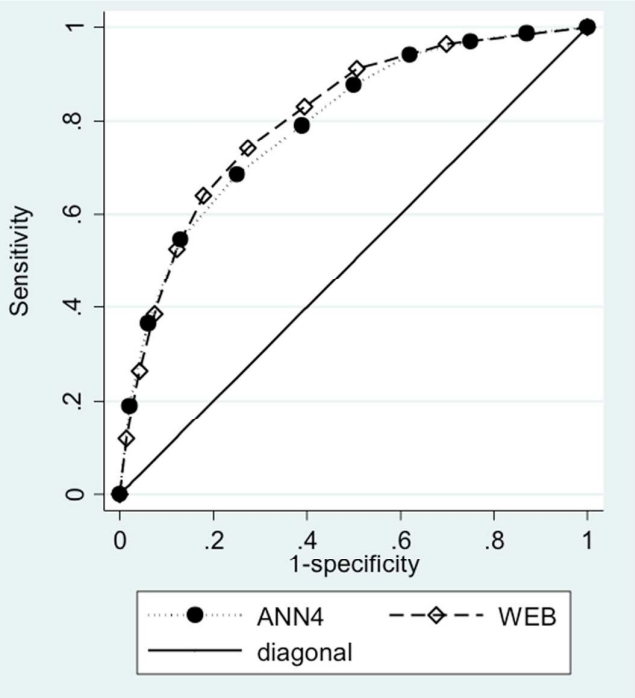
not normally distributed. Statistical analyses were performed with STATA (StataCorp) and Statistica (Statsoft Inc).

RESULTS

During the two years of the study period a total of 6556 nerve conduction tests were requested for CTS. We excluded from the analysis patients who already had known CTS prior to visiting the website, those having tests for follow-up purposes or who had already had treatment for one hand and were returning for management of the second. This left 4899 patients who were referred during their initial presentation with suspected CTS. Of these 2821 (58%) completed the website questionnaire before testing and of this group 166 (5%) then failed to actually attend or cancelled their appointments. Referrals came predominantly (82%) direct from primary care physicians.

The diagnostic performance of the web-based questionnaire is summarized in the receiver operating characteristic curve shown in figure 1 where one of the ROC curves for the paper version is also shown for comparison. The two curves are almost indistinguishable and the changes to the questionnaire involved in presenting it on a website do not appear to have altered its diagnostic properties.

FIGURE 1



To demonstrate the possible utility of the website, figure two shows the proportions of patients in 10% bands by website diagnostic score who prove to have CTS and also the distribution of website scores in the population of patients referred to the Canterbury neurophysiology department for a suspected diagnosis of CTS. 26% of all referrals have website diagnostic scores <20% and 81% of this group of patients have normal median nerve conduction studies.

FIGURE 2

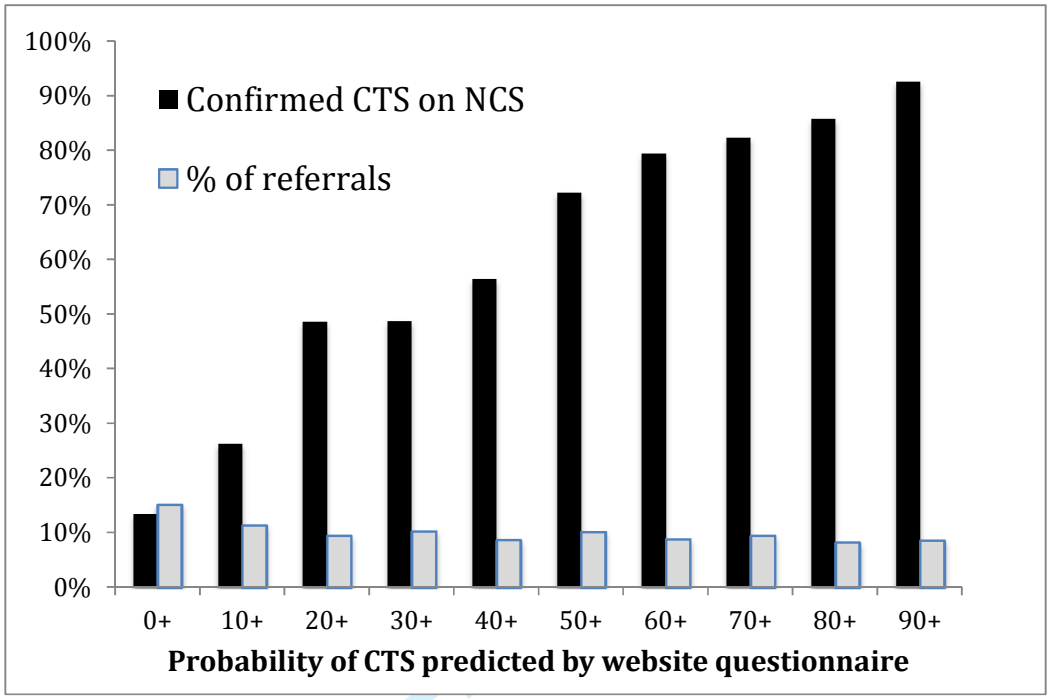


Figure three illustrates the relationship between the website score and the severity of CTS demonstrated in the worst hand. The relationship is highly statistically significant but weak (Pearson r=0.30 p<0.0001).

FIGURE 3

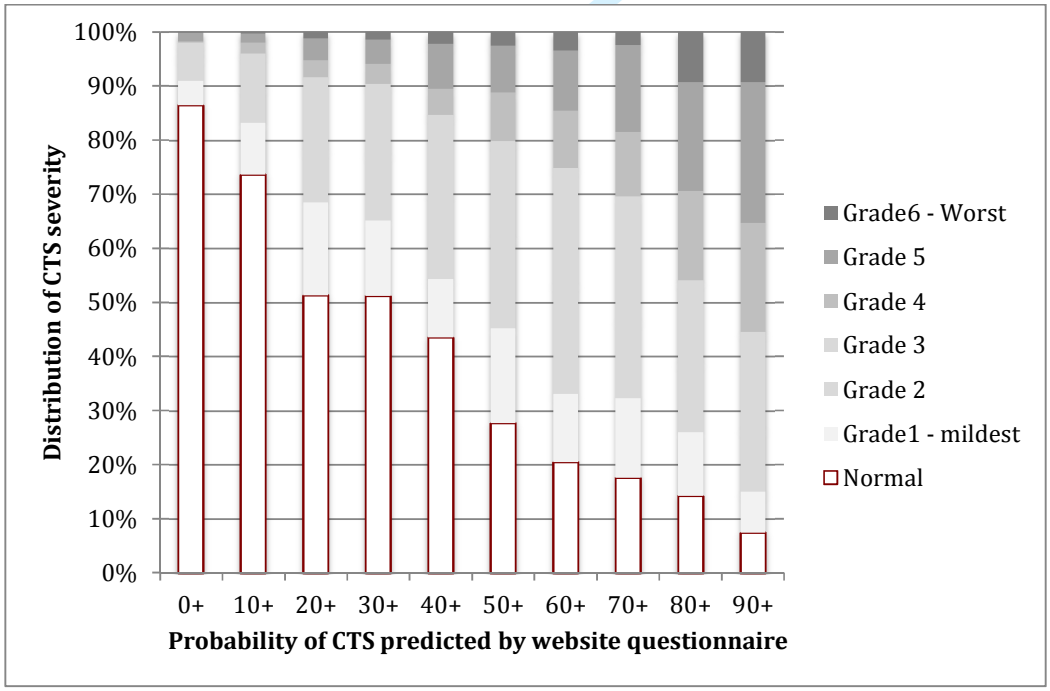
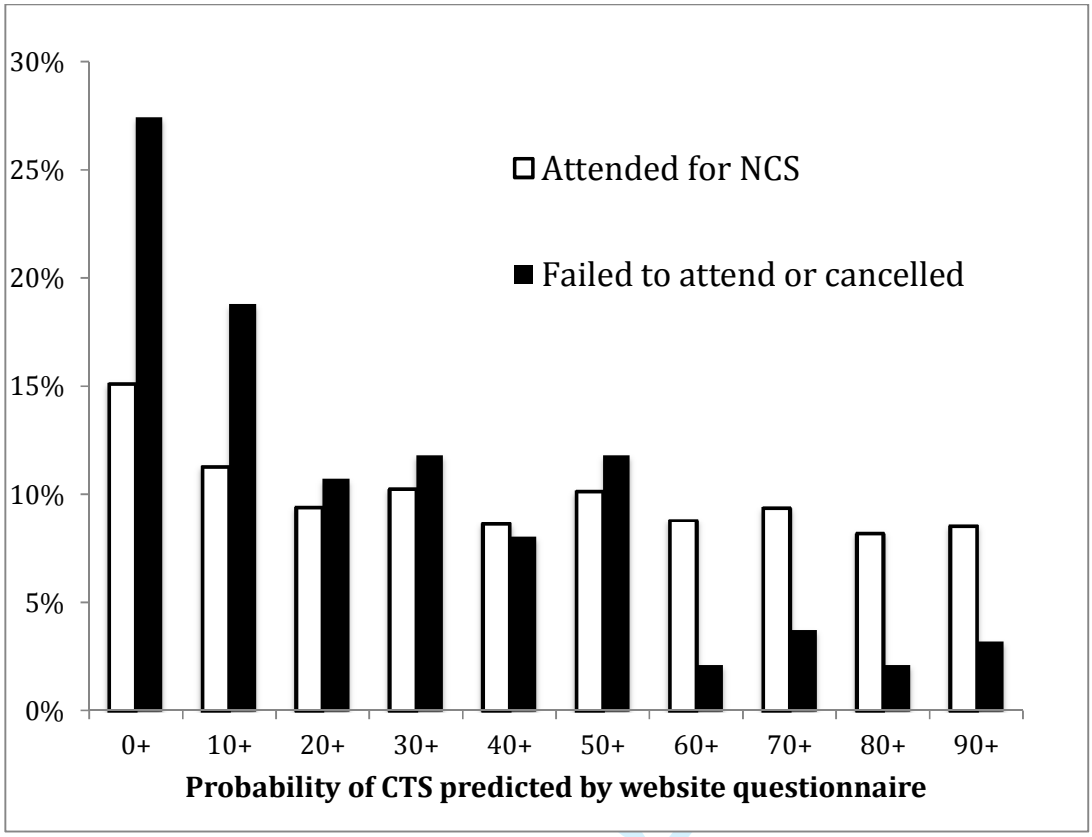


Figure 4 shows the distribution of website scores in the 166 patients who did not attend for testing compared to that of the 2655 who did attend. There is a marked tendency for the non-attenders to have lower scores (Mann Whitney U-test, adjusted Z=-4.57, p<0.00001)

FIGURE 4



DISCUSSION

The website questionnaire performs as expected in predicting neurophysiological confirmation of the diagnosis of CTS. It has a slight overall tendency to underestimate the probability of disease except with the very highest scores. Thus a group of patients with scores from 0-9% (average 5%) turn out to have a 13% prevalence of neurophysiological abnormalities consistent with CTS while a group with an average score of 95% have a 92% prevalence of CTS. The explanation for this lies partly in the fact that we are comparing the website predictions against nerve conduction studies which are known to have significant false positive and false negative rates in the diagnosis of CTS. At the lower end of the range of website scores, the great majority of NCS abnormalities are mild (figure 2) and it is likely that, in a significant proportion of these patients, their clinical problem is not CTS, even if they do have slight evidence of median nerve impairment on nerve conduction studies. Conversely at the higher end of the range it is likely that many patients with very high symptom scores are examples of false negative nerve conduction studies. We have recently begun examining these high scoring, NCS-

negative patients with ultrasound imaging and some of them do show evidence of CTS using that method.

There are some methodological limitations to the current study. The patients were recruited because their general practitioner was sufficiently suspicious of a possible diagnosis of CTS that they were referred for neurophysiological testing and they are therefore not necessarily representative of all patients with hand and arm symptoms and the results presented here may not be achieved by patients who have simply stumbled upon the website by themselves. Secondly this is not a blinded study. The patients themselves saw their website diagnostic score as soon as they completed the questionnaire and were thus immediately informed of the likelihood of CTS before attending for testing. We received some telephone calls from patients with low scores during the study period asking whether it was still worth them attending for the test if it was unlikely to show evidence of CTS. We tried to encourage these patients to attend anyway as we were trying to assess the performance of the site in a full range of patients but there is a significant excess of low scoring patients in the group who failed to attend and it is likely that, despite our efforts to encourage people to attend, directing patients to the website has already led some low scoring patients to decide for themselves not to attend. Conversely, patients with high scores were more likely to attend. We also did not blind the technical staff performing the nerve conduction studies to the website scores but nerve conduction studies are a relatively objective measure and the results are not likely to have been greatly influenced by the operators knowledge of the website scores.

The role of nerve conduction studies in the diagnosis and management of carpal tunnel syndrome has been the subject of much debate and a view that they are diagnostically superfluous, or even contraindicated, when the clinician is certain of the diagnosis is widespread in hand surgery circles at least in the UK (ref BHS guidelines), though in the USA widely agreed guidelines recommend the use of NCS in all cases before surgery. The Ontario hand surgery group have made the Bayesian argument that, when the clinical probability of CTS is either very high or very low, then performing NCS is not likely to change the post-test probability of CTS significantly, whatever the result. They proposed a clinical scoring system, the CTS-7, which, like our website questionnaire, is intended to quantify the clinical certainty of diagnosis in CTS so that an approach of only testing patients with intermediate probabilities of CTS could be adopted.[7] This tool however has not been prospectively evaluated in real patients and is not available for patients to use on the internet. We have compared a simple scoring system proposed in the UK [8] against our models and found it to be significantly less accurate in predicting CTS.[4] A similar method to ours, using a logistic regression analysis, has been adopted in a South American patient group and claims good diagnostic performance but has not yet been prospectively evaluated in new patients and again is not readily available to the general public.[9] None of these alternate tools have yet demonstrated that their results are related to the neurophysiological severity of CTS, nor to the prognosis for surgical or conservative treatment.

Confirming or refuting the diagnosis is not the only, or even the primary, reason for carrying out nerve conduction studies in suspected CTS. The evaluation of the physiological severity of nerve damage, for prognosis and for follow-up when

treatment is unsuccessful, and the detection of other nerve problems such as underlying polyneuropathy are probably more important in clinically obvious cases than the diagnostic result of the test.

We believe that we have created a tool which can be used by patients with hand symptoms to derive a baseline probability that they have CTS and which is sufficiently accurate to be used to guide initial patient management. Units wishing to restrict the use of nerve conduction studies for diagnosis to patients in whom there is uncertainty can now obtain an objective measure of the clinical likelihood of CTS on which to base decisions about investigation and treatment. We recommend that, whenever carpal tunnel syndrome is suspected in primary care, the patient should be directed to carpal-tunnel.net to complete the questionnaire at home, or, if unable to access the internet themselves, aided to complete the questionnaire by ancilliary staff in the practice. Management can then begin with an objective probability that CTS is the correct diagnosis.

COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

CONTRIBUTORSHIP

Jeremy D P Bland – interpreted all of the nerve conduction studies, extracted and collated all of the data from the website and neurophysiology department databases, and wrote the first draft of the main body text of the article.

Peter Weller – devised the neural network algorithm used to analyse the patient input questionnaire data and contributed to the writing of the main body text.

Stephan Rudolpher – devised the logistic regression model used to analyse the patient input questionnaire data, carried out the statistical assessment of the extracted data for this paper, and contributed to editing the body text.

DATA SHARING STATEMENT

No extra data directly relating to this assessment is available but the questionnaire used to collect data from patients is freely available online at http://carpal-tunnel.net

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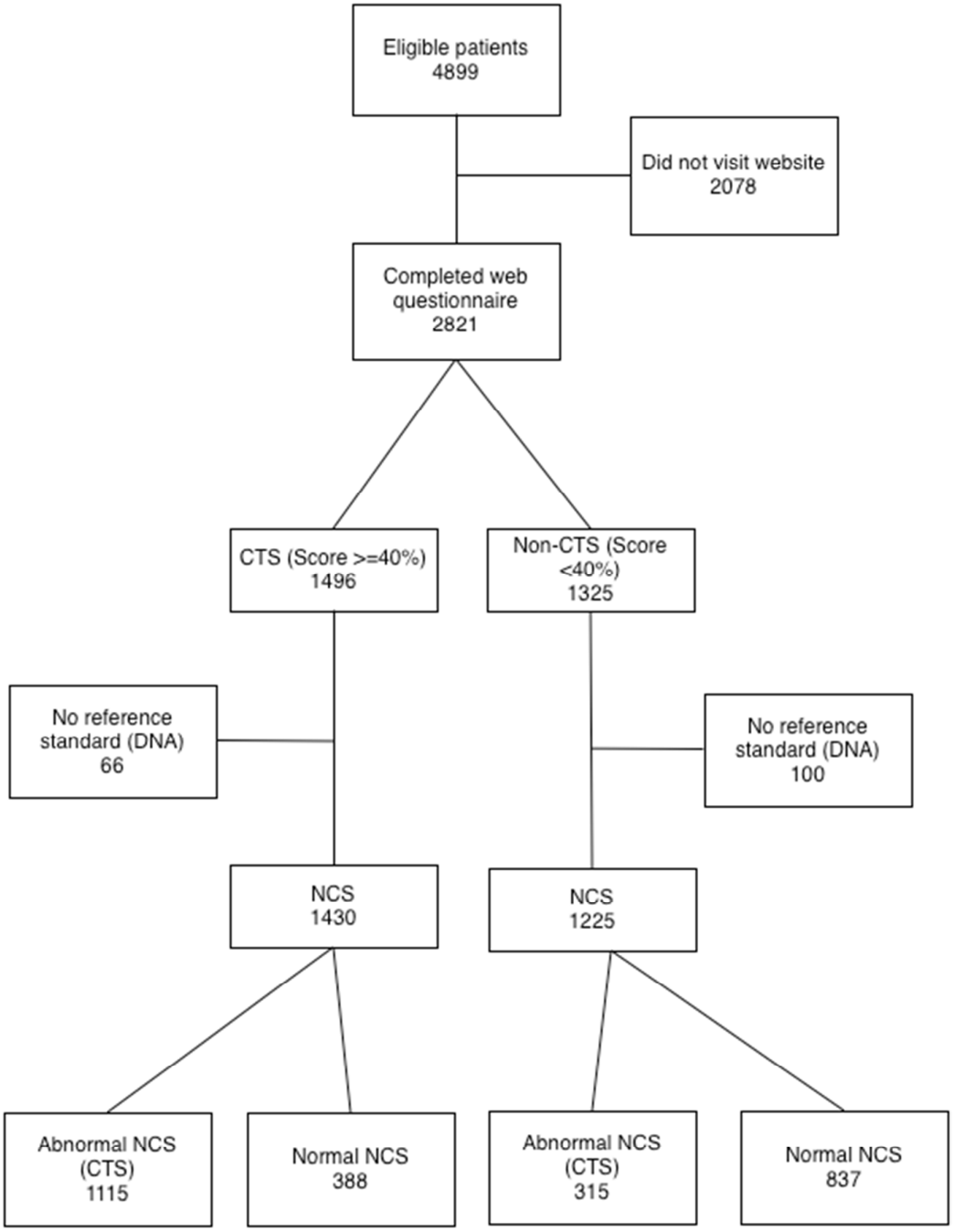
STARD Flow Diagram



BMJ submission guidelines require this diagram. In main body of our paper we have chosen to represent the sensitivity and specificity of the website questionnaire using an ROC curve, which allows one to trade off sensitivity vs specificity by choosing different cut-off scores for different purposes. It does not however lend itself to a STARD flow diagram. We have therefore constructed this flow diagram for an arbitrarily chosen cut-off point in the web score of <40% as representative of 'not likely to be CTS'. Many other such diagrams could be produced.

STARD checklist for the reporting of studies of diagnostic accuracy.

First official version, January 2003.

Section and Topic	Item #		On page #
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	Title
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	1
METHODS			
Participants	3	Describe the study population: The inclusion and exclusion criteria, setting and locations where the data were collected.	2
	4	Describe participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?	2 borderline
	5	Describe participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in items 3 and 4? If not, specify how participants were further selected.	2
	6	Describe data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	Prospective
Test methods	7	Describe the reference standard and its rationale.	2
	8	Describe technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.	2
	9	Describe definition of and rationale for the units, cutoffs and/or categories of the results of the index tests and the reference standard.	2
	10	Describe the number, training and expertise of the persons executing and reading the index tests and the reference standard.	NA !
	11	Describe whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.	NA
Statistical methods	12	Describe methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).	2
	13	Describe methods for calculating test reproducibility, if done.	NA
RESULTS			
Participants	14	Report when study was done, including beginning and ending dates of recruitment.	2
	15	Report clinical and demographic characteristics of the study population (e.g. age, sex, spectrum of presenting symptoms, comorbidity, current treatments, recruitment centers).	—
	16	Report the number of participants satisfying the criteria for inclusion that did or did not undergo the index tests and/or the reference standard; describe why participants failed to receive either test (a flow diagram is strongly recommended).	3
Test results	17	Report time interval from the index tests to the reference standard, and any treatment administered between.	—
	18	Report distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	Fig 3
	19	Report a cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard.	- Expand on ROC curve.
	20	Report any adverse events from performing the index tests or the reference standard.	None
Estimates	21	Report estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	- ROC curve
	22	Report how indeterminate results, missing responses and outliers of the index tests were handled.	NA
	23	Report estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	—
	24	Report estimates of test reproducibility, if done.	—
DISCUSSION	25	Discuss the clinical applicability of the study findings.	6

BMJ Open

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Figures – 4, Tables 1

Word Count – 3519 excluding references

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Objective – To confirm the accuracy of a diagnostic questionnaire for carpal tunnel syndrome (CTS) when presented via a public website rather than on paper

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Setting – Sub regional neurophysiology laboratory serving a population of 700,000 in East Kent, UK

Participants – 2821 individuals who were able to complete an online diagnostic questionnaire out of 4899 referred for initial diagnostic testing for new presentations with suspected CTS from April 2011 to March 2013. No exclusions were made on grounds of age, gender or coincident pathology.

Main outcome measure – Nerve conduction results confirming CTS. The severity of median nerve impairment demonstrated was also assessed using a validated neurophysiological scale.

Results – The web based questionnaire accurately estimates the probability of CTS being confirmed on nerve conduction studies. Using a website diagnostic score of >=40% as an example cut-off value the questionnaire achieves 78% sensitivity and 68% specificity in predicting the finding of evidence of CTS on nerve conduction studies. The web based version of the diagnostic questionnaire was as accurate as the original paper version with an area under the receiver operating characteristic curve of 0.79. There was also a significant correlation between the diagnostic score given by the website and the severity of CTS with higher scores being associated with greater nerve dysfunction ($r=0.3$, $p<0.00001$).

Conclusion – Completion of the symptom questionnaire on the website by patients at home provides a prediction of the likelihood of CTS which is sufficiently accurate to be used in initial planning of investigation and treatment.

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Strengths

- Prospective design
- Large numbers
- Objective confirmation of diagnosis using best available current methods
- Unselected patient population

Weaknesses

- Lack of blinding

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The diagnosis of carpal tunnel syndrome (CTS) is often straightforward, requiring no more than listening to the patient's description of the characteristic timing and distribution of the symptoms and a focused examination of the hands to look for obvious signs. Nevertheless there remains no reliable 'gold standard' test for the diagnosis and an extensive literature exists debating the relative merits of clinical diagnosis, nerve conduction studies (NCS), imaging methods and response to treatment as elements of the definition for the syndrome. NCS and imaging produce results which can be quantified and analysed for their diagnostic properties but studies of clinical diagnosis, which are comparatively rare, generally approach it as a binary opinion – the patient either does, or does not have, CTS. This does not fairly represent the subtlety of clinical opinion which encompasses a range of certainty rather than being an absolute. Human beings however are rarely able to express their degree of certainty consistently in numerical form for analysis. We have been interested for some years in whether the answers to a questionnaire relating to the symptoms could be analysed mathematically to arrive at an estimate of the probability of CTS, based on the same information used by clinicians, but which would be reproducible and quantifiable so that it could be compared with the results of diagnostic tests.

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METHODS

The collection of a standardized clinical history by questionnaire has been standard practice in the Canterbury department of clinical neurophysiology for 20 years and it was not considered necessary to seek either ethics committee approval nor written patient consent for transferring this process of data collection from paper to the

website. Completion of the questionnaire on the web takes 20-30 minutes. The website questionnaire contains a variety of questions which may or may not be of use in making a diagnosis of CTS as we have experimented with a large number of variables at different times in the mathematical models. Although in classical logistic regression it is possible to prune variables which prove to be of limited use in the overall model it is much harder to do this for the neural network model and the entire historically developed question set is therefore still collected. There are also some questions in the overall website questionnaire which are there to support other studies rather than being purely included for diagnostic purposes. Patients retained the option of completing the paper form of the questionnaire if they did not wish to use the web version. The analysis of the anonymised data for this study was however approved by the regional ethics committee.

Patients referred for investigation of possible carpal tunnel syndrome to the sub-regional department of clinical neurophysiology in Canterbury, Kent, UK between 1.4.2011 and 1.4.2013 were invited, in their appointment letter, to visit the website at http://www.carpal-tunnel.net prior to their appointment and to complete the questionnaire. To do this, patients had to create a user account on the website but we recommended that they create a user identity which did not reveal who they were to third party observers viewing interactions on the site. We provided them, also in the neurophysiology appointment letter, with a reference number to be entered into the site registration page which would identify them uniquely to us. The key data table linking these reference numbers to patient identities is not stored anywhere in the website but is kept in the internal computerized records of the neurophysiology department within the secure boundaries of the hospital IT systems.

On attending the neurophysiology department, patients were asked whether they had been able to complete the questionnaire on the website and those who had not been able to do so were given the original paper version to complete. All patients then had nerve conduction studies performed for CTS according to guidelines published by the American Association of Neuromuscular and Electrodiagnostic Medicine.[5] The nerve conduction results were graded using the Canterbury severity scale for CTS [6], which represents the changes in sensory and motor nerve conduction velocities and amplitudes as a numerical scale increasing in severity from 0 (no abnormality) to 6 (extremely severe CTS). No exclusions were applied on grounds of age, gender or coincident pathology.

In order to work with the patient rather than the hand as the unit of analysis each patient was classified using the nerve conduction results as either CTS, if either hand showed at least grade 1 CTS, or normal. The diagnostic scores produced by the website were then compared against the presence or absence of CTS and also, in a secondary analysis, against the neurophysiological severity of the worst hand. Finally, as 6% of patients fail to attend our clinic after completing the web questionnaire, we looked at the distribution of website diagnostic scores to see if this subpopulation differed from the patients who did attend for testing.

The web-based questionnaire does not return a binary verdict – CTS, yes or no – but a percentage probability of CTS. The sensitivity and specificity of the questionnaire

can therefore be tuned to favour the detection of more disease or the exclusion of more patients who do not prove to have CTS by adjusting the score which is taken as indicating CTS. This variable diagnostic performance was calculated across the full range of scores by constructing a receiver operating characteristic curve for comparison with that derived for the paper questionnaire previously. The relationship between the web questionnaire score and the neurophysiological severity of CTS in the worst hand of patients who did have evidence of CTS was assessed using Pearson correlation. The website scores of patients who did, and did not , attend for testing were compared with non-parametric tests as the scores are not normally distributed. Statistical analyses were performed with STATA (StataCorp) and Statistica (Statsoft Inc).

RESULTS

During the two years of the study period a total of 6556 nerve conduction tests were requested for CTS. We excluded from the analysis patients who already had known CTS prior to visiting the website, those having tests for follow-up purposes or who had already had treatment for one hand and were returning for management of the second. This left 4899 patients who were referred during their initial presentation with suspected CTS. Of these 2821 (58%) completed the website questionnaire before testing and of this group 166 (5%) then failed to actually attend or cancelled their appointments. Referrals came predominantly (82%) direct from primary care physicians. Patients who completed the questionnaire were predominantly female (1884/2821 = 67% female, with a mean age of 54.2 years as expected from the epidemiology of carpal tunnel syndrome. The 166 patients who failed to attend for testing having completed the questionnaire were younger, average age 49 years. The patients who did not complete the questionnaire online tended to be slightly older, mean age 58 years, but had a similar profile of NCS results and symptom severity when tested with 43% having normal nerve conduction studies.

The diagnostic performance of the web-based questionnaire is summarized in the receiver operating characteristic curve shown in figure 1 where one of the ROC curves for the paper version of the questionnaire in 2640 prospectively assessed patients is also shown for comparison.[4] The two curves are almost indistinguishable and the changes to the questionnaire involved in presenting it on a website do not appear to have altered its diagnostic properties.

To demonstrate the possible utility of the website, Table 1 shows the proportions of patients in 10% bands by website diagnostic score who prove to have CTS and also the distribution of website scores in the population of patients referred to the Canterbury neurophysiology department for a suspected diagnosis of CTS. 26% of all referrals have website diagnostic scores <20% and 81% of this group of patients have normal median nerve conduction studies.

Figure two illustrates the relationship between the website score and the severity of CTS demonstrated in the worst hand. Each column shows the proportions of patients in one range of website diagnostic scores who proved to have nerve conduction studies of each grade of severity, normalized to 100%. Thus, of 401 patients with a website diagnostic score of <10%, 87% had normal NCS, 4% grade1, 4% grade 2, 2%

grade 3, 0.2% grade 4, 1% grade 5 and 0.2% grade 6) The relationship is highly statistically significant but weak (Pearson r=0.30 p<0.0001).

Figure 3 shows the distribution of website scores in the 166 patients who did not attend for testing compared to that of the 2655 who did attend. There is a marked tendency for the non-attenders to have lower scores (Mann Whitney U-test, adjusted Z=-4.57, p<0.00001)

DISCUSSION

The website questionnaire performs as expected in predicting neurophysiological confirmation of the diagnosis of CTS. It has a slight overall tendency to underestimate the probability of disease except with the very highest scores. Thus a group of patients with scores from 0-9% (average 5%) turn out to have a 13% prevalence of neurophysiological abnormalities consistent with CTS while a group with an average score of 95% have a 92% prevalence of CTS. The explanation for this lies partly in the fact that we are comparing the website predictions against nerve conduction studies which are known to have significant false positive and false negative rates in the diagnosis of CTS. Many estimates of the false negative and false positive rates have been made, one study for example finding 30% false negative and 18% false negative rates in comparison to clinical diagnosis,[7] but in the absence of any true gold standard for the diagnosis of CTS it is impossible to know the true rates. At the lower end of the range of website scores, the great majority of NCS abnormalities are mild (figure 2) and it is likely that, in a significant proportion of these patients, their clinical problem is not CTS, even if they do have slight evidence of median nerve impairment on nerve conduction studies. Conversely at the higher end of the range it is likely that many patients with very high symptom scores are examples of false negative nerve conduction studies. We have recently begun examining these high scoring, NCS-negative patients with ultrasound imaging and some of them do show evidence of CTS using that method.

There are some methodological limitations to the current study. The patients were recruited because their general practitioner was sufficiently suspicious of a possible diagnosis of CTS that they were referred for neurophysiological testing and they are therefore not necessarily representative of all patients with hand and arm symptoms and the results presented here may not be achieved by patients who have simply stumbled upon the website by themselves. Secondly this is not a blinded study. The patients themselves saw their website diagnostic score as soon as they completed the questionnaire and were thus immediately informed of the likelihood of CTS before attending for testing. We received some telephone calls from patients with low scores during the study period asking whether it was still worth them attending for the test if it was unlikely to show evidence of CTS. We tried to encourage these patients to attend anyway as we were trying to assess the performance of the site in a full range of patients but there is a significant excess of low scoring patients in the group who failed to attend and it is likely that, despite our efforts to encourage people to attend, directing patients to the website has already led some low scoring patients to decide for themselves not to attend. Conversely, patients with high scores

were more likely to attend. We also did not blind the technical staff performing the nerve conduction studies to the website scores but nerve conduction studies are a relatively objective measure and the results are not likely to have been greatly influenced by the operators knowledge of the website scores.

The role of nerve conduction studies in the diagnosis and management of carpal tunnel syndrome has been the subject of much debate and a view that they are diagnostically superfluous, or even contraindicated, when the clinician is certain of the diagnosis is widespread in hand surgery circles at least in the UK (ref BHS guidelines), though in the USA widely agreed guidelines recommend the use of NCS in all cases before surgery. The Ontario hand surgery group have made the Bayesian argument that, when the clinical probability of CTS is either very high or very low, then performing NCS is not likely to change the post-test probability of CTS significantly, whatever the result. They proposed a clinical scoring system, the CTS-7, which, like our website questionnaire, is intended to quantify the clinical certainty of diagnosis in CTS so that an approach of only testing patients with intermediate probabilities of CTS could be adopted.[8] This tool however has not been prospectively evaluated in real patients and is not available for patients to use on the internet. We have compared a simple scoring system proposed in the UK [9] against our models and found it to be significantly less accurate in predicting CTS.[4] A similar method to ours, using a logistic regression analysis, has been adopted in a South American patient group and claims good diagnostic performance but has not yet been prospectively evaluated in new patients and again is not readily available to the general public.[10] None of these alternate tools have yet demonstrated that their results are related to the neurophysiological severity of CTS, nor to the prognosis for surgical or conservative treatment.

Confirming or refuting the diagnosis is not the only, or even the primary, reason for carrying out nerve conduction studies in suspected CTS. The evaluation of the physiological severity of nerve damage, for prognosis and for follow-up when treatment is unsuccessful, and the detection of other nerve problems such as underlying polyneuropathy are probably more important in clinically obvious cases than the diagnostic result of the test.

We believe that we have created a tool which can be used by patients with hand symptoms to derive a baseline probability that they have CTS and which is sufficiently accurate to be used to guide initial patient management. Units wishing to restrict the use of nerve conduction studies for diagnosis to patients in whom there is uncertainty can now obtain an objective measure of the clinical likelihood of CTS on which to base decisions about investigation and treatment. We recommend that, whenever carpal tunnel syndrome is suspected in primary care, the patient should be directed to carpal-tunnel.net to complete the questionnaire at home, or, if unable to access the internet themselves, aided to complete the questionnaire by ancilliary staff in the practice. Management can then begin with an objective probability that CTS is the correct diagnosis.

COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

CONTRIBUTORSHIP

Jeremy D P Bland – interpreted all of the nerve conduction studies, extracted and collated all of the data from the website and neurophysiology department databases, and wrote the first draft of the main body text of the article.

Peter Weller – devised the neural network algorithm used to analyse the patient input questionnaire data and contributed to the writing of the main body text.

Stephan Rudolfer – devised the logistic regression model used to analyse the patient input questionnaire data, carried out the statistical assessment of the extracted data for this paper, and contributed to editing the body text.

DATA SHARING STATEMENT

No additional data available.

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Table 1

Numbers of subjects categorized by diagnostic score on the website in 10% bands, the percentage of the total patient population falling in each of these bands, and the number and percentage of patients in each band showing evidence of CTS on nerve conduction studies

Website Score	Subjects	% of total	CTS	% of group
0-9%	401	15%	54	13%
10-19%	300	11%	79	26%
20-29%	251	9%	122	49%
30-39%	273	10%	133	49%
40-49%	230	9%	130	57%
50-59%	270	10%	195	72%
60-69%	235	9%	187	80%
70-79%	250	9%	206	82%
80-89%	218	8%	187	86%
>90%	227	9%	210	93%
TOTAL	2655			

FIGURE LEGENDS

Figure 1

Receiver operating characteristic curve illustrating the diagnostic sensitivity and specificity of the website questionnaire for neurophysiologically defined carpal tunnel syndrome with varying cut-off scores from 0-100% (diamonds - WEB). For comparison the equivalent curve for the paper version of the questionnaire is shown (circles – ANN4). The area under these curves is 0.79. The diagonal line would indicate a test with no ability to discriminate between disease and normal.

Figure 2

The relationship between the website score and the severity of CTS demonstrated in the worst hand. Each column shows the proportions of patients in one 10% range of website diagnostic scores who proved to have nerve conduction studies of each grade of severity, normalized to 100%. Thus, of 401 patients with a website diagnostic score of <10%, 87% had normal NCS, 4% grade1, 4% grade 2, 2% grade 3, 0.2% grade 4, 1% grade 5 and 0.2% grade 6)

Figure 3

Distributions of website diagnostic scores (in 10% bands) in patients who attended for testing (white bars), compared to those who failed to attend (black bars)

Figure 4

STARD flow diagram for the study using an arbitrary cut-off score on the website questionnaire of 40% as indicating carpal tunnel syndrome.

Prospective analysis of the accuracy of diagnosis of carpal tunnel syndrome using a web based questionnaire

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Honorary Research Fellow in Biostatistics,
Centre for Health Informatics, City University London, London, EC1V 0HB, Peter Weller
Senior Lecturer in Medical Informatics

Correspondence to: Jeremy.Bland@nhs.net

Contributors – Peter Weller and Stephan Rudolfer created the mathematical models used to analyse the questionnaire and performed the statistical analysis of the prospectively collected data. Jeremy Bland reported and graded all of the nerve conduction studies, and collated the questionnaire data from the website. All three authors contributed to the drafting of the paper and jointly act as guarantors.

Figures – 4

Word Count – 3507~~2671~~ excluding references

Keywords – Carpal Tunnel Syndrome, Diagnosis, World-wide-web, Questionnaire, Sensitivity and Specificity

ABSTRACT

Objective – To confirm the accuracy of a diagnostic questionnaire for carpal tunnel syndrome (CTS) when presented via a public website rather than on paper

Design – Prospective comparison of the probability of CTS as assessed by the web-based questionnaire at http://www.carpal-tunnel.net with the results of nerve conduction studies

Setting – Sub regional neurophysiology laboratory serving a population of 700,000 in East Kent, UK

Participants – 2821 individuals who were able to complete an online diagnostic questionnaire out of 4899~~All individuals~~ referred for initial diagnostic testing for new presentations with suspected CTS from April 2011 to March 2013. No exclusions were made on grounds of age, gender or coincident pathology.

Main outcome measure – Nerve conduction results confirming CTS. The severity of median nerve impairment demonstrated was also assessed using a validated neurophysiological scale.

Results – The web based questionnaire accurately estimates the probability of CTS being confirmed on nerve conduction studies. Using a website diagnostic score of >=40% as an example cut-off value the questionnaire achieves 78% sensitivity and 68% specificity in predicting the finding of evidence of CTS on nerve conduction studies. The web based version of the diagnostic questionnaire was as accurate as the original paper version with an area under the receiver operating characteristic curve of 0.79.~~-~~ There was also a significant correlation between the diagnostic score given by the website and the severity of CTS with higher scores being associated with greater nerve dysfunction (r=0.3, p<0.00001).

Conclusion – Completion of the symptom questionnaire on the website by patients at home provides a prediction of the likelihood of CTS which is sufficiently accurate to be used in initial planning of investigation and treatment.

Comment [JB1]: Order of presentation of results amended at suggestion of reviewer 4 to emphasise the accuracy of he questionnaire rather than the comparison with the earlier data relating to the paper version

STRENGTHS AND LIMITATIONS OF THIS STUDY

Strengths

- Prospective design
- Large numbers
- Objective confirmation of diagnosis using best available current methods
- Unselected patient population

Weaknesses

- Lack of blinding

WHAT THIS PAPER ADDS

What is already known on this subject

Self completed patient questionnaires have been used to make diagnoses with acceptable accuracy compared to conventional clinical assessments for screening purposes previously. Such tools have not been made widely available to patients on the internet

What this study adds

This study shows that a self completed diagnostic questionnaire on a public website can make the diagnosis of carpal tunnel syndrome with considerable accuracy in patients with hand symptoms. It also demonstrates that a mathematical analysis of a questionnaire can yield a verifiably accurate estimate of the probability of a disease being present.~~shows that the analysis of the questionnaire using mathematical approaches can give a diagnosis in terms of probability which can be validated against an objective test as an accurate assessment.~~

INTRODUCTION

The diagnosis of carpal tunnel syndrome (CTS) is often straightforward, requiring no more than listening to the patient's description of the characteristic timing and distribution of the symptoms and a focused examination of the hands to look for obvious signs. Nevertheless there remains no reliable 'gold standard' test for the diagnosis and an extensive literature exists debating the relative merits of clinical diagnosis, nerve conduction studies (NCS), imaging methods and response to treatment as elements of the definition for the syndrome. NCS and imaging produce results which can be quantified and analysed for their diagnostic properties but studies of clinical diagnosis, which are comparatively rare, generally approach it as a binary opinion – the patient either does, or does not have, CTS. This does not fairly represent the subtlety of clinical opinion which encompasses a range of certainty rather than being an absolute. Human beings however are rarely able to express their degree of certainty consistently in numerical form for analysis. We have been interested for some years in whether the answers to a questionnaire relating to the symptoms could be analysed mathematically to arrive at an estimate of the probability of CTS, based on the same information used by clinicians, but which would be reproducible and quantifiable so that it could be compared with the results of diagnostic tests.

Interest in standardized questionnaires for diagnosis is not new and some questionnaires have been shown to achieve good agreement with conventional clinical diagnosis for common conditions, for example in asthma[1] or restless legs syndrome[2] but these tools are not widely available to patients to use unaided.

An early version of our diagnostic questionnaire achieved 79% sensitivity and ~~-~~55% specificity for the diagnosis of CTS when the result of nerve conduction studies was used as the reference standard.[3] We refined and extended the questionnaire and by 2011 the paper version had grown to 6 pages and improved to 96% sensitivity and 50% specificity in predicting the NCS result when tuned to optimize sensitivity in order to avoid missing treatable disease. [4] Not only was the paper questionnaire cumbersome but the mathematical methods used to analyse the answers – a logistic regression model and an artificial neural network – required the aid of a computer to calculate the probability of CTS. We therefore created a website on which patients could complete the questionnaire and which would perform the calculations immediately it was completed. Our assessments of the performance of the questionnaire however had been made using the paper version and we could not be sure that it would perform in the same way when presented in online format. This study therefore prospectively analyses the diagnostic accuracy of the web-based version of the questionnaire, again using the results of nerve conduction studies as the reference standard for CTS.

METHODS

The collection of a standardized clinical history by questionnaire has been standard practice in the Canterbury department of clinical neurophysiology for 20 years and it was not considered necessary to seek either ethic~~sal~~ committee approval nor written patient consent for transferring this process of data collection from paper to

the website. Completion of the questionnaire on the web takes 20-30 minutes. The website questionnaire contains a variety of questions which may or may not be of use in making a diagnosis of CTS as we have experimented with a large number of variables at different times in the mathematical models. Although in classical logistic regression it is possible to prune variables which prove to be of limited use in the overall model it is much harder to do this for the neural network model and the entire historically developed question set is therefore still collected. There are also some questions in the overall website questionnaire which are there to support other studies rather than being purely included for diagnostic purposes. -Patients retained the option of completing the paper form of the questionnaire if they did not wish to use the web version. The analysis of the anonymised data for this study was however approved by the regional ethics committee.

Patients referred for investigation of possible carpal tunnel syndrome to the sub-regional department of clinical neurophysiology in Canterbury, Kent, UK between 1.4.2011 and 1.4.2013 were invited, in their appointment letter, to visit the website at http://www.carpal-tunnel.net prior to their appointment and to complete the questionnaire. To do this, patients had to create a user account on the website but we recommended that they create a user identity which did not reveal who they were to third party observers viewing interactions on the site. We provided them, also in the neurophysiology appointment letter, with a reference number to be entered into the site registration page which would identify them uniquely to us. The key data table linking these reference numbers to patient identities is not stored anywhere in the website but is kept in the internal computerized records of the neurophysiology department within the secure boundaries of the hospital IT systems.

On attending the neurophysiology department, patients were asked whether they had been able to complete the questionnaire on the website and those who had not been able to do so were given the original paper version to complete. All patients then had nerve conduction studies performed for CTS according to guidelines published by the American Association of Neuromuscular and Electrodiagnostic Medicine.[5] The nerve conduction results were graded using the Canterbury severity scale for CTS [6], which represents the changes in sensory and motor nerve conduction velocities and amplitudes as a numerical scale increasing in severity from 0 (no abnormality) to 6 (extremely severe CTS). No exclusions were applied on grounds of age, gender or coincident pathology.

In order to work with the patient rather than the hand as the unit of analysis each patient was classified using the nerve conduction results as either CTS, if either hand showed at least grade 1 CTS, or normal. The diagnostic scores produced by the website were then compared against the presence or absence of CTS and also, in a secondary analysis, against the neurophysiological severity of the worst hand. Finally, as 6% of patients fail to attend our clinic after completing the web questionnaire, we looked at the distribution of website diagnostic scores to see if this subpopulation differed from the patients who did attend for testing.

The web-based questionnaire does not return a binary verdict – CTS, yes or no – but a percentage probability of CTS. The sensitivity and specificity of the questionnaire

can therefore be tuned to favour the detection of more disease or the exclusion of more patients who do not prove to have CTS by adjusting the score which is taken as indicating CTS. This variable diagnostic performance was calculated across the full range of scores by constructing a receiver operating characteristic curve for comparison with that derived for the paper questionnaire previously. The relationship between the web questionnaire score and the neurophysiological severity of CTS in the worst hand of patients who did have evidence of CTS was assessed using Pearson correlation. The website scores of patients who did, and did not , attend for testing were compared with non-parametric tests as the scores are not normally distributed. Statistical analyses were performed with STATA (StataCorp) and Statistica (Statsoft Inc).

RESULTS

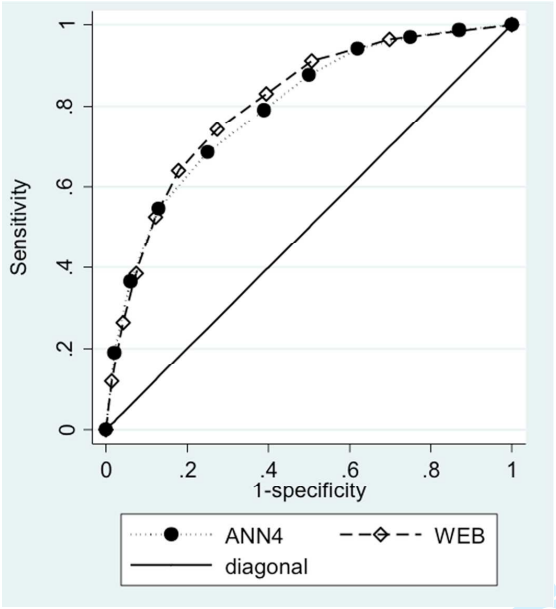
During the two years of the study period a total of 6556 nerve conduction tests were requested for CTS. We excluded from the analysis patients who already had known CTS prior to visiting the website, those having tests for follow-up purposes or who had already had treatment for one hand and were returning for management of the second. This left 4899 patients who were referred during their initial presentation with suspected CTS. Of these 2821 (58%) completed the website questionnaire before testing and of this group 166 (5%) then failed to actually attend or cancelled their appointments. Referrals came predominantly (82%) direct from primary care physicians. Patients who completed the questionnaire were predominantly female (1884/2821 = 67% female, with a mean age of 54.2 years as expected from the epidemiology of carpal tunnel syndrome. The 166 patients who failed to attend for testing having completed the questionnaire were younger, average age 49 years. The patients who did not complete the questionnaire online tended to be slightly older, mean age 58 years, but had a similar profile of NCS results and symptom severity when tested with 43% having normal nerve conduction studies.

The diagnostic performance of the web-based questionnaire is summarized in the receiver operating characteristic curve shown in figure 1 where one of the ROC curves for the paper version of the questionnaire in 2640 prospectively assessed patients is also shown for comparison.[4] The two curves are almost indistinguishable and the changes to the questionnaire involved in presenting it on a website do not appear to have altered its diagnostic properties.

Comment [JB2]: Reviewer two though we might not be able to improve the paper regarding the issue of the characteristics of the patients who did not complete the questionnaire online. In fact I have been able to go back to the database and check the demographic and clinical data for the patients who did not complete the online questionnaire. Apart from being a little older they are identical in gender, symptom severity on Boston CTS questionnaires and NCS results, both in terms of confirming/refuting CTS and assessing severity. I therefore think that the web based questionnaire is demonstrating its properties in a relatively unbiased sample. I have added some text alluding briefly to this but not all of the comparisons in the text.

Comment [JB3]: Reviewer two feels that we should have made the patients complete both the paper and website based versions and that this would have been better methodology. Quite apart from the tedium inflicted on the patients we feel that the answers given to whichever version was completed second may have been distorted by having just answered the same questions in the other medium, introducing a different kind of bias from a learning effect. It would not have been practicable to randomize the order of presentation of the two forms of the questionnaire because of the logistics of running the neurophysiology service.

FIGURE 1



To demonstrate the possible utility of the website, Table 1~~figure two~~ shows the proportions of patients in 10% bands by website diagnostic score who prove to have CTS and also the distribution of website scores in the population of patients referred to the Canterbury neurophysiology department for a suspected diagnosis of CTS. 26% of all referrals have website diagnostic scores <20% and 81% of this group of patients have normal m~~m~~edian nerve conduction studies.

Table 1

Website Score	Subjects	% of total	CTS	% of group
0-9%	401	15%	54	13%
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20-29%	251	9%	122	49%
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50-59%	270	10%	195	72%
60-69%	235	9%	187	80%
70-79%	250	9%	206	82%
80-89%	218	8%	187	86%
>90%	227	9%	210	93%
TOTAL	2655			

~~FIGURE 2~~

Comment [JB4]: The editors suggested replacing bar charts with tables where possible and reviewer 2 had difficulty with the labeling of figure 2 so this hs been replaced with a table showing the same data.

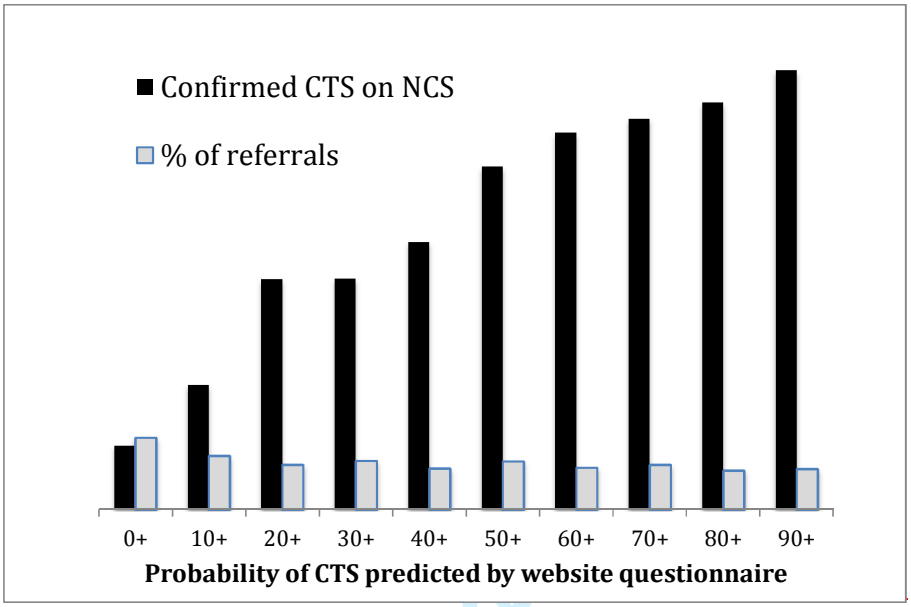


Figure two~~three~~ illustrates the relationship between the website score and the severity of CTS demonstrated in the worst hand. Each column shows the proportions of patients in one range of website diagnostic scores who proved to have nerve conduction studies of each grade of severity, normalized to 100%. Thus, of 401 patients with a website diagnostic score of <10%, 87% had normal NCS, 4% grade1, 4% grade 2, 2% grade 3, 0.2% grade 4, 1% grade 5 and 0.2% grade 6) The relationship is highly statistically significant but weak (Pearson r=0.30 p<0.0001).

FIGURE ~~3~~2

Comment [JB5]: Reviewer 2 also had difficulty with this figure, which does contain a great deal of data. It will also make a very complex table in which it will be harder to see the relationship in a dense array of numbers. For the moment I have added some further explanation of how it is constructed to the text. If BMJ open are able to handle a colour figure then it may be better to use a colour scale for severity rather than grey scale

Comment [JB6]: Reviewer two asked why this correlation is so weak – I think the answer is that it just is sorry! Nerve conduction studies do not measure CTS directly. They measure a physiological property which happens to be fairly well correlated with the presence of CTS but they are known to be only loosely correlated with conventional assessments of severity. It is not really possible to go into the relationships between different measures of severity in CTS in the current paper.

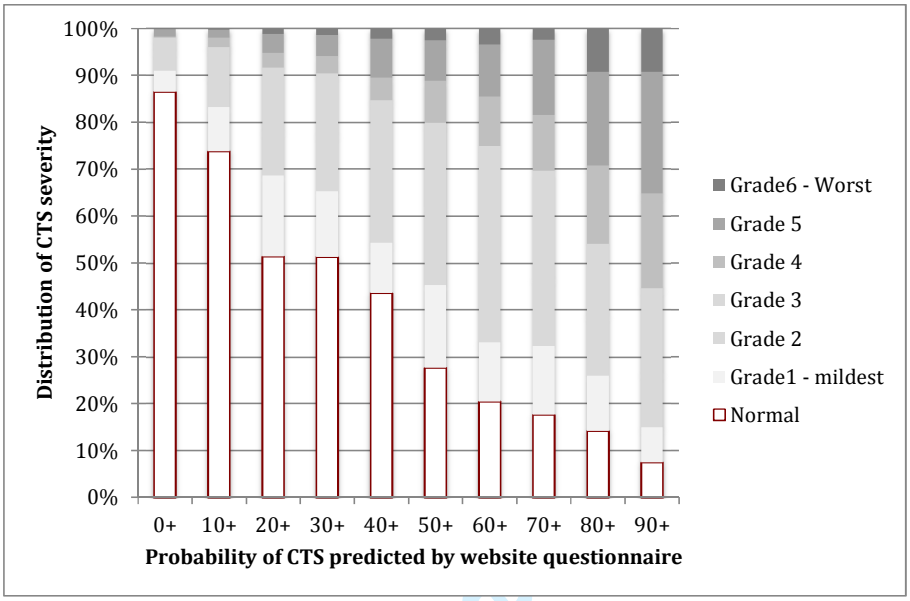
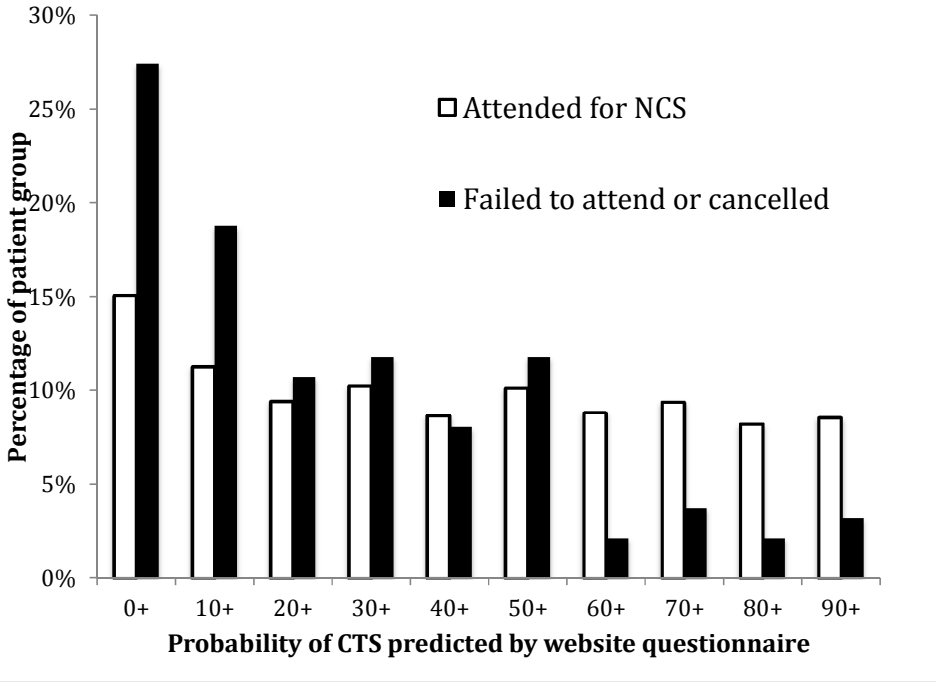
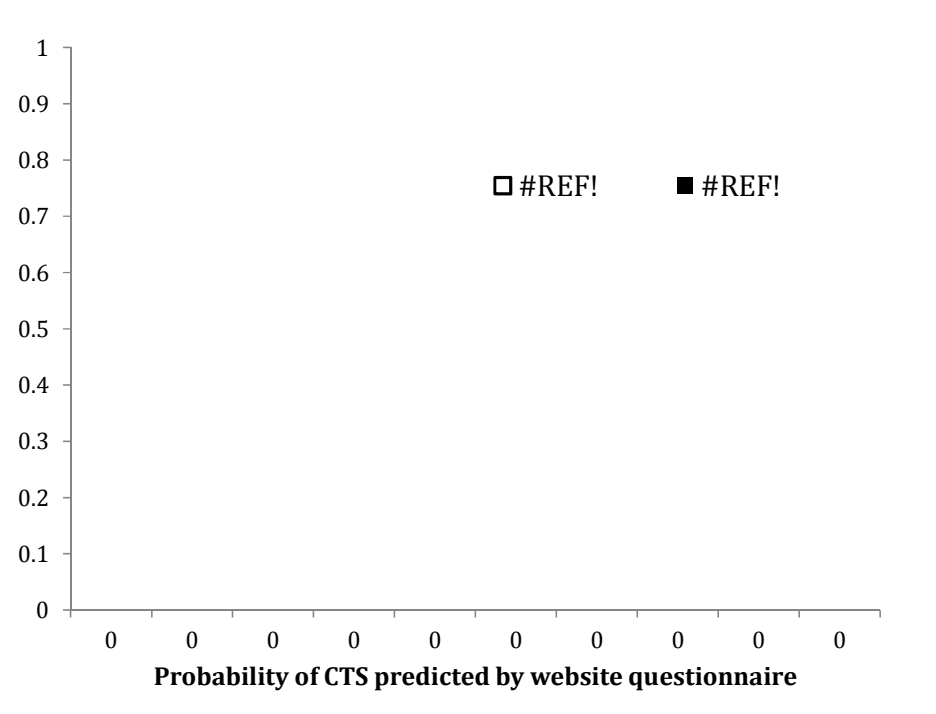


Figure 34 shows the distribution of website scores in the 166 patients who did not attend for testing compared to that of the 2655 who did attend. There is a marked tendency for the non-attenders to have lower scores (Mann Whitney U-test, adjusted Z=-4.57, p<0.00001)

FIGURE 34





Comment [JB7]: For the editors – the purpose of this histogram is to illustrate the different distributions of scores in the two populations. It does this better as a figure than as a data table.

DISCUSSION

The website questionnaire performs as expected in predicting neurophysiological confirmation of the diagnosis of CTS. It has a slight overall tendency to underestimate the probability of disease except with the very highest scores. Thus a group of patients with scores from 0-9% (average 5%) turn out to have a 13% prevalence of neurophysiological abnormalities consistent with CTS while a group with an average score of 95% have a 92% prevalence of CTS. The explanation for this lies partly in the fact that we are comparing the website predictions against nerve conduction studies which are known to have significant false positive and false negative rates in the diagnosis of CTS. Many estimates of the false negative and false positive rates have been made, one study for example finding 30% false negative and 18% false negative rates in comparison to clinical diagnosis,[7] but in the absence of any true gold standard for the diagnosis of CTS it is impossible to know the true rates. At the lower end of the range of website scores, the great majority of NCS abnormalities are mild (figure 2) and it is likely that, in a significant proportion of these patients, their clinical problem is not CTS, even if they do have slight evidence of median nerve impairment on nerve conduction studies. Conversely at the higher end of the range it is likely that many patients with very high symptom scores are examples of false negative nerve conduction studies. We have recently begun examining these high scoring, NCS-negative patients with ultrasound imaging and some of them do show evidence of CTS using that method.

There are some methodological limitations to the current study. The patients were recruited because their general practitioner was sufficiently suspicious of a possible diagnosis of CTS that they were referred for neurophysiological testing and they are therefore not necessarily representative of all patients with hand and arm symptoms and the results presented here may not be achieved by patients who have simply stumbled upon the website by themselves. Secondly this is not a blinded study. The patients themselves saw their website diagnostic score as soon as they completed the questionnaire and were thus immediately informed of the likelihood of CTS before attending for testing. We received some telephone calls from patients with low scores during the study period asking whether it was still worth them attending for the test if it was unlikely to show evidence of CTS. We tried to encourage these patients to attend anyway as we were trying to assess the performance of the site in a full range of patients but there is a significant excess of low scoring patients in the group who failed to attend and it is likely that, despite our efforts to encourage people to attend, directing patients to the website has already led some low scoring patients to decide for themselves not to attend. Conversely, patients with high scores were more likely to attend. We also did not blind the technical staff performing the nerve conduction studies to the website scores but nerve conduction studies are a relatively objective measure and the results are not likely to have been greatly influenced by the operators knowledge of the website scores.

The role of nerve conduction studies in the diagnosis and management of carpal tunnel syndrome has been the subject of much debate and a view that they are diagnostically superfluous, or even contraindicated, when the clinician is certain of the diagnosis is widespread in hand surgery circles at least in the UK (ref BHS

Comment [JB8]: Reviewer two has raised some points which I am happy to address but which I am not sure should be included in the current paper as they are not really the topic of this study

1) Would it be better to dispense with NCS in patients with a very high clinical probability of CTS? This has been suggested by Brent Graham and others. The problem of course lies in deciding who exactly has a high probability of CTS. The web based questionnaire allows one to put a precise probability figure to this whereas other studies rely on clinical judgement which is known to be highly variable – especially in primary care. For the purposes of the current study the NCS HAD to be done to validate the questionnaire but one could now make a case for dispensing with them in patients with a high score on the website. It should be noted however that the purpose of carrying out NCS in ordinary clinical practice for CTS is not really to make or refute the diagnosis but is more about evaluating severity, detecting other pathology and forming a baseline for when treatment fails, especially surgery.

2) Should clinical examination have been carried out before NCS? The only clinical examination findings which are reliable in NCS are the presence of thenar wasting and weakness and fixed sensory loss in the fingers. Provocative tests such as TInel's sign are known to perform poorly in diagnostic terms, especially in non-expert hands. By the time thenar wasting has appeared the prognosis for carpal tunnel surgery is already significantly impaired and CTS really needs to be detected before this, when physical examination is almost entirely useless.

3) Other CTS scores? – The Boston questionnaire (which is in any case included within the questionnaire at carpal-tunnel.net) was designed to evaluate severity of symptoms not to make the diagnosis. The best known simple diagnostic score in the UK is that proposed by Kamath. We have evaluated ours against that and the questionnaire at carpal-tunnel.net has noticeably better performance – see our previous paper.

4) Response to carpal tunnel release as a gold standard ?– I am afraid this is not at all satisfactory. Many patients with undoubted carpal tunnel syndrome have poor outcomes from carpal tunnel surgery (about 8% in my series) and patients with many self limiting conditions may improve after carpal tunnel decompression, producing false positives.

... [1]

guidelines), though in the USA widely agreed guidelines recommend the use of NCS in all cases before surgery. The Ontario hand surgery group have made the Bayesian argument that, when the clinical probability of CTS is either very high or very low, then performing NCS is not likely to change the post-test probability of CTS significantly, whatever the result. They proposed a clinical scoring system, the CTS-7, which, like our website questionnaire, is intended to quantify the clinical certainty of diagnosis in CTS so that an approach of only testing patients with intermediate probabilities of CTS could be adopted.[8] This tool however has not been prospectively evaluated in real patients and is not available for patients to use on the internet. We have compared a simple scoring system proposed in the UK [9] against our models and found it to be significantly less accurate in predicting CTS.[4] A similar method to ours, using a logistic regression analysis, has been adopted in a South American patient group and claims good diagnostic performance but has not yet been prospectively evaluated in new patients and again is not readily available to the general public.[10] None of these alternate tools have yet demonstrated that their results are related to the neurophysiological severity of CTS, nor to the prognosis for surgical or conservative treatment.

Confirming or refuting the diagnosis is not the only, or even the primary, reason for carrying out nerve conduction studies in suspected CTS. The evaluation of the physiological severity of nerve damage, for prognosis and for follow-up when treatment is unsuccessful, and the detection of other nerve problems such as underlying polyneuropathy are probably more important in clinically obvious cases than the diagnostic result of the test.

We believe that we have created a tool which can be used by patients with hand symptoms to derive a baseline probability that they have CTS and which is sufficiently accurate to be used to guide initial patient management. Units wishing to restrict the use of nerve conduction studies for diagnosis to patients in whom there is uncertainty can now obtain an objective measure of the clinical likelihood of CTS on which to base decisions about investigation and treatment. We recommend that, whenever carpal tunnel syndrome is suspected in primary care, the patient should be directed to carpal-tunnel.net to complete the questionnaire at home, or, if unable to access the internet themselves, aided to complete the questionnaire by ancilliary staff in the practice. Management can then begin with an objective probability that CTS is the correct diagnosis.

COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

CONTRIBUTORSHIP

Jeremy D P Bland – interpreted all of the nerve conduction studies, extracted and collated all of the data from the website and neurophysiology department databases, and wrote the first draft of the main body text of the article.

Peter Weller – devised the neural network algorithm used to analyse the patient input questionnaire data and contributed to the writing of the main body text.

Stephan Rudol~~fpl~~er – devised the logistic regression model used to analyse the patient input questionnaire data, carried out the statistical assessment of the extracted data for this paper, and contributed to editing the body text.

DATA SHARING STATEMENT

No extra data directly relating to this assessment is available but the questionnaire used to collect data from patients is freely available online at http://carpal-tunnel.net

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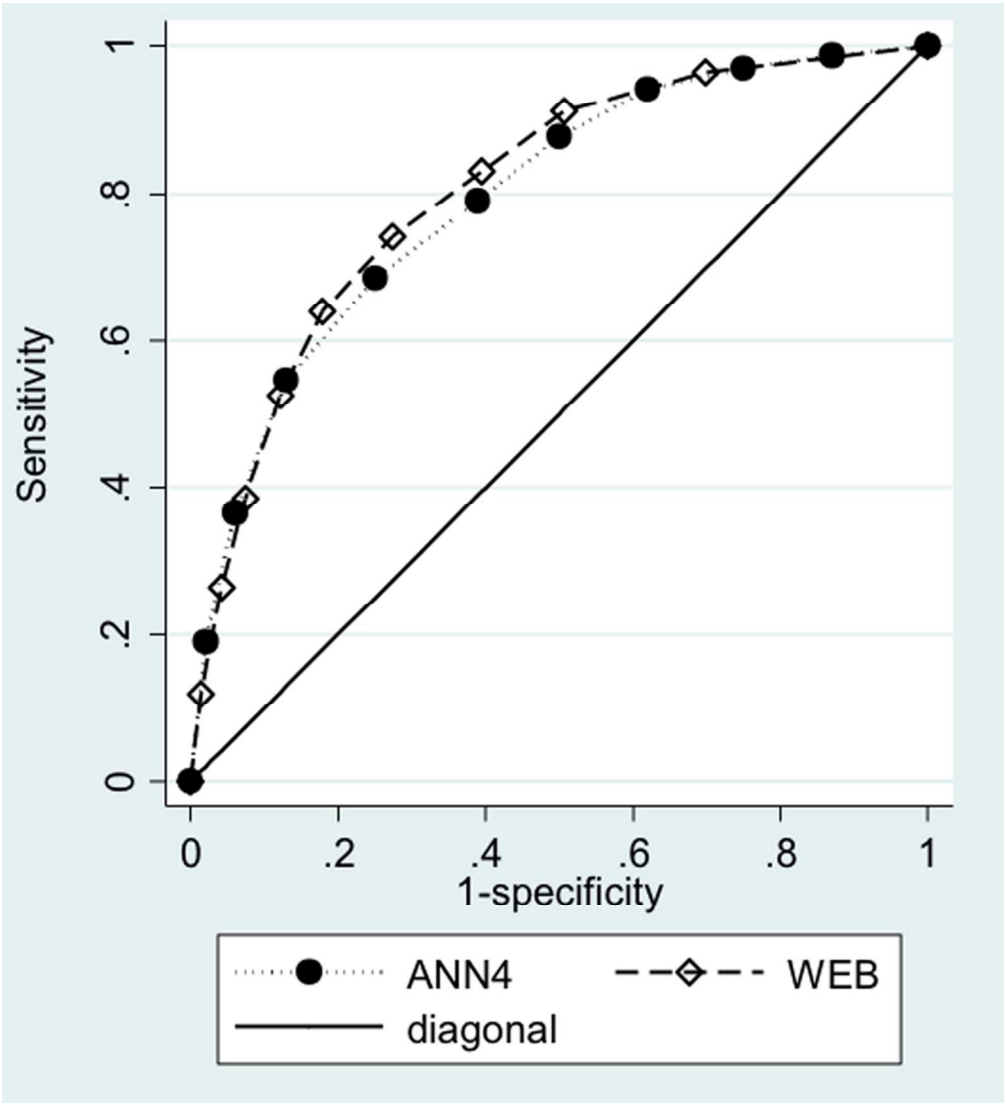
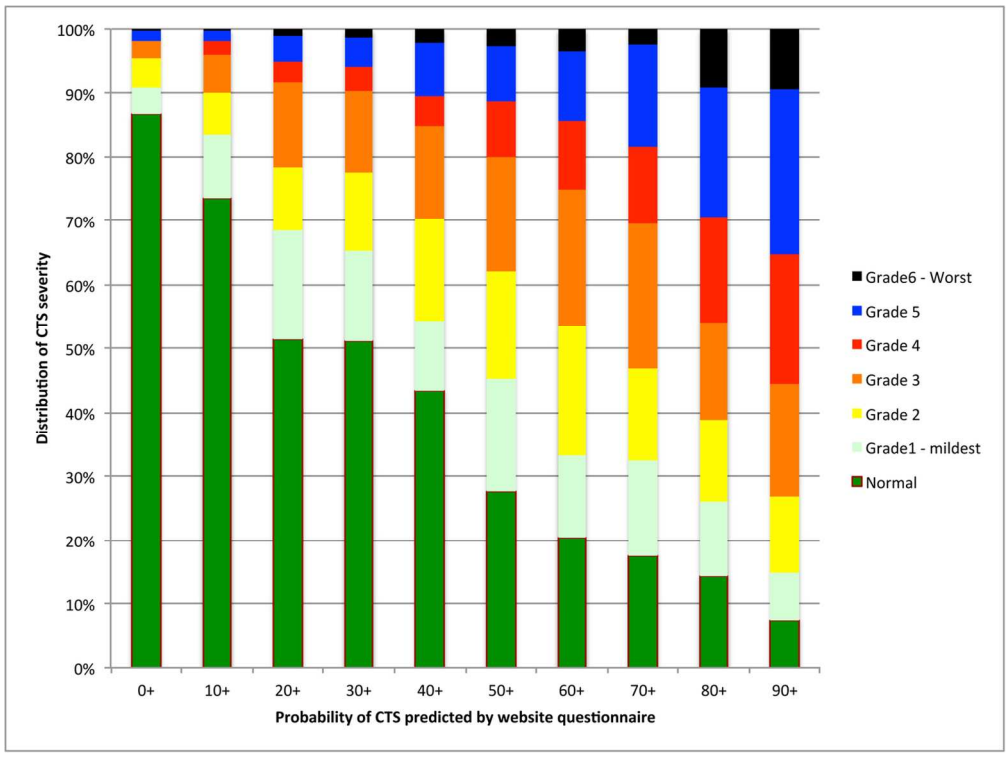
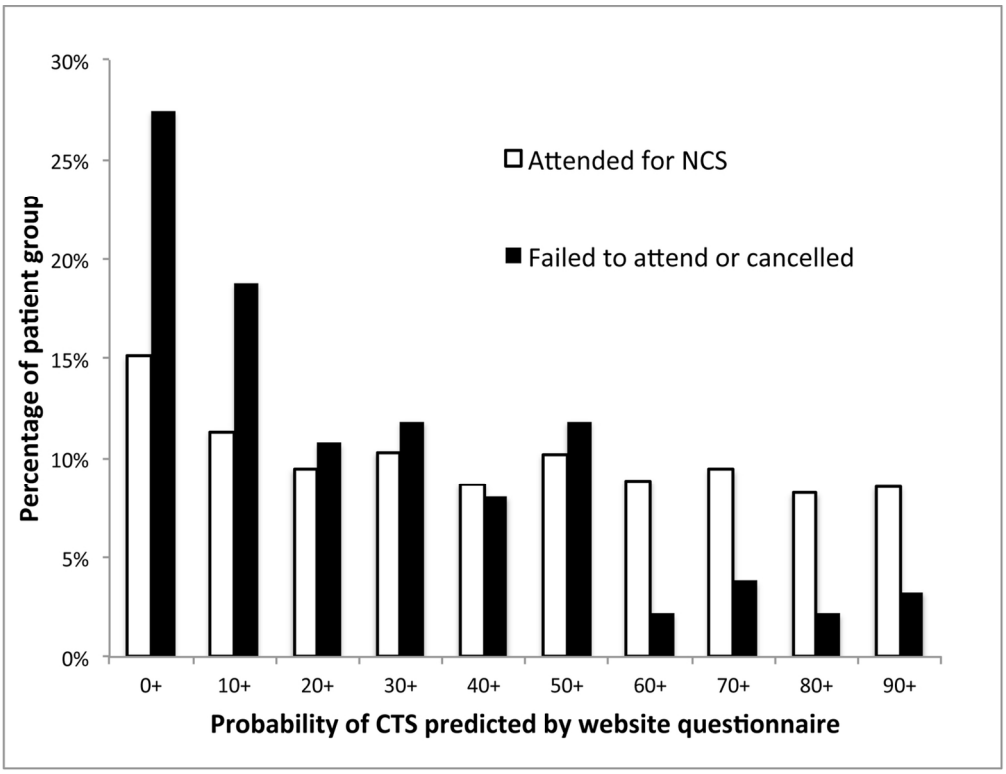


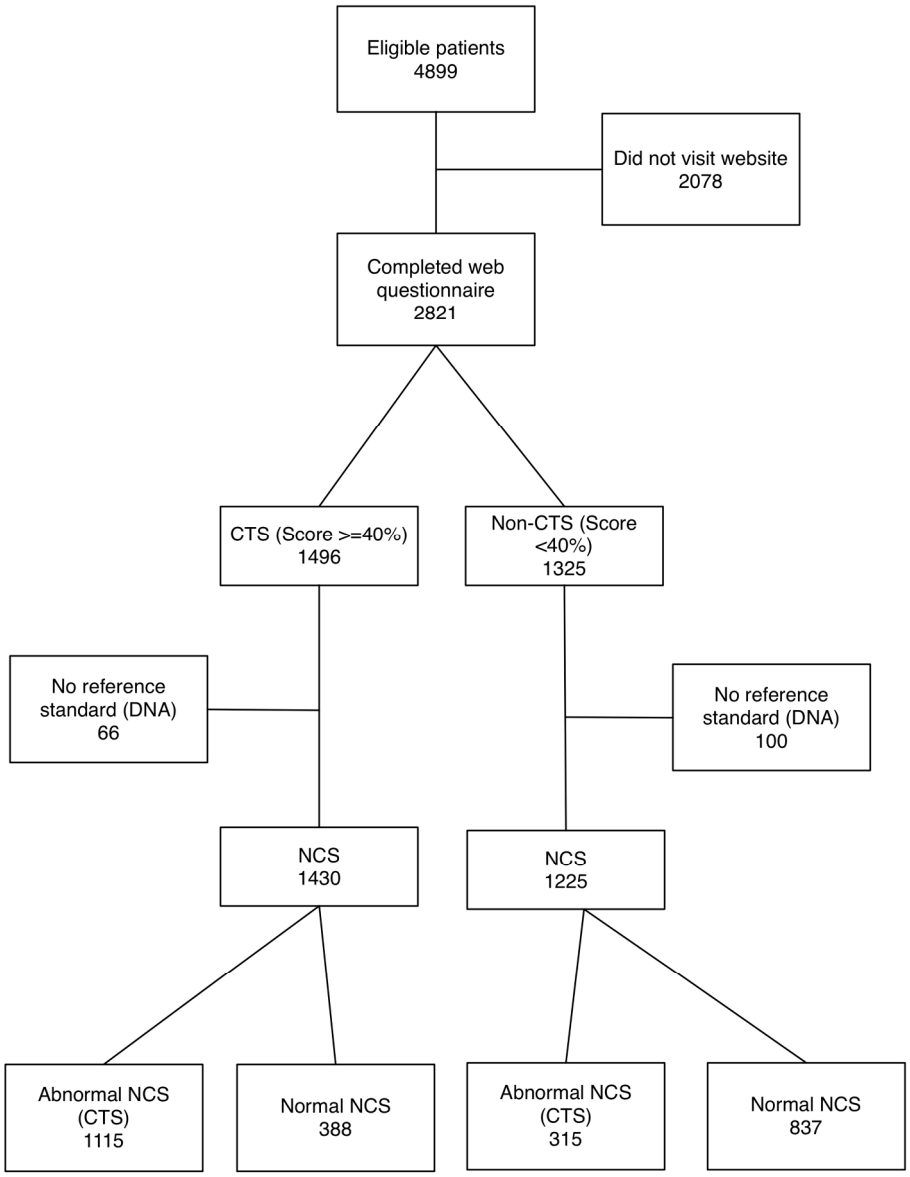
Receiver operating characteristic curve illustrating the diagnostic sensitivity and specificity of the website questionnaire for neurophysiologically defined carpal tunnel syndrome with varying cut-off scores from 0-100% (diamonds - WEB). For comparison the equivalent curve for the paper version of the questionnaire is shown (circles – ANN4). The area under these curves is 0.79. The diagonal line would indicate a test with no ability to discriminate between disease and normal.
89x98mm (300 x 300 DPI)



The relationship between the website score and the severity of CTS demonstrated in the worst hand. Each column shows the proportions of patients in one 10% range of website diagnostic scores who proved to have nerve conduction studies of each grade of severity, normalized to 100%. Thus, of 401 patients with a website diagnostic score of <10%, 87% had normal NCS, 4% grade1, 4% grade 2, 2% grade 3, 0.2% grade 4, 1% grade 5 and 0.2% grade 6)
129x96mm (300 x 300 DPI)



Distributions of website diagnostic scores (in 10% bands) in patients who attended for testing (white bars), compared to those who failed to attend (black bars)
132x101mm (300 x 300 DPI)



STARD flow diagram for the study using an arbitrary cut-off score on the website questionnaire of 40% as indicating carpal tunnel syndrome.
223x286mm (300 x 300 DPI)

STARD checklist for the reporting of studies of diagnostic accuracy.

First official version, January 2003.

Section and Topic	Item #		On page #
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	Title
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	1
METHODS			
Participants	3	Describe the study population: The inclusion and exclusion criteria, setting and locations where the data were collected.	2
	4	Describe participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?	2 borderline
	5	Describe participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in items 3 and 4? If not, specify how participants were further selected.	2
	6	Describe data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	Prospective
Test methods	7	Describe the reference standard and its rationale.	2
	8	Describe technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.	2
	9	Describe definition of and rationale for the units, cutoffs and/or categories of the results of the index tests and the reference standard.	2
	10	Describe the number, training and expertise of the persons executing and reading the index tests and the reference standard.	NA !
	11	Describe whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.	NA
Statistical methods	12	Describe methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).	2
	13	Describe methods for calculating test reproducibility, if done.	NA
RESULTS			
Participants	14	Report when study was done, including beginning and ending dates of recruitment.	2
	15	Report clinical and demographic characteristics of the study population (e.g. age, sex, spectrum of presenting symptoms, comorbidity, current treatments, recruitment centers).	—
	16	Report the number of participants satisfying the criteria for inclusion that did or did not undergo the index tests and/or the reference standard; describe why participants failed to receive either test (a flow diagram is strongly recommended).	3
Test results	17	Report time interval from the index tests to the reference standard, and any treatment administered between.	—
	18	Report distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	Fig 3
	19	Report a cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard.	- Expand on ROC curve.
	20	Report any adverse events from performing the index tests or the reference standard.	None
Estimates	21	Report estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	- ROC curve
	22	Report how indeterminate results, missing responses and outliers of the index tests were handled.	NA
	23	Report estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	—
	24	Report estimates of test reproducibility, if done.	—
DISCUSSION	25	Discuss the clinical applicability of the study findings.	6