

## PREDICTORS FOR IMMEDIATE AND GLOBAL RESPONSES TO CHIROPRACTIC MANIPULATION OF THE CERVICAL SPINE

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### ABSTRACT

**Objective:** Patients with nonspecific musculoskeletal disorders may vary in their response to treatment. This study set out to identify the predictors for either improvement or worsening in symptoms for which cervical spine manipulation is indicated.

**Method:** A large prospective study recorded details on patients, their presenting symptoms, and type of treatment. At the end of the consultation, any immediate improvement or worsening in presenting symptoms was noted. At the follow-up visit, information was collected on the patients' self-reported improvement.

**Results:** Data were collected from 28 807 treatment consultations (in 19 722 patients) and 13 873 follow-up treatments. The presenting symptoms of "neck pain," "shoulder, arm pain," "reduced neck, shoulder, arm movement, stiffness," "headache," "upper, mid back pain," and "none or one presenting symptom" emerged in the final model as significant predictors for an immediate improvement. The presence of any 4 of these predictors raised the probability for an immediate improvement in presenting symptoms after treatment from 70% to ~95%. With regard to immediate worsening, "neck pain," "shoulder, arm pain," "headache," "numbness, tingling upper limbs," "upper, mid back pain," and "fainting, dizziness, light-headedness" emerged as predictors; and the presence of any 4 of these raised the probability for immediate worsening from 4.4% to ~12%. For global improvement, only 2 predictors were identified; but these did not enhance the postprediction probability.

**Conclusions:** This study is the first attempt to identify variables that can predict immediate outcomes in terms of improvement and worsening of presenting symptoms, and global improvement, after cervical spine manipulation. The predictor variables were strongest for immediate improvement. (*J Manipulative Physiol Ther* 2008;31:172-183)

**Key Indexing Terms:** *Manipulation; Spinal; Neck Pain; Prediction; Treatment Outcomes; Chiropractic*

**M**echanical neck disorders are very common; approximately 15% to 70% of the adult population can recall experiencing an episode of neck pain or stiffness in their lifetime.<sup>1</sup> In most cases, neck pain defies the identification of any pathological cause, leading to the term *nonspecific*. It is likely that within this group of nonspecific patients, a number of subgroups exist and that these groups may differ in their responses to treatment. Although there is evidence<sup>2,3</sup> that spinal manipulation is an effective treatment of nonspecific neck pain, this evidence is not always consistent; one explanation may be the inclusion of different

subgroups of patients in clinical trials giving overall effects that mask individual subgroup responses.

It is becoming clear that among patients where subgroups probably exist, there is a need to identify those patients who are likely to respond to treatment. Predicting outcome of treatment is a clinical tool that has the potential not only to improve the design of clinical trials but also the efficiency of the management of these patients. These so-called clinical prediction rules generally consist of combinations of variables obtained from self-reported measures and/or clinical examinations and can assist with identifying subgroups of patients that can be expected to benefit from treatment.

Some work has been done on clinical prediction rules as guides to the manipulative treatment of neck and back pain patients.<sup>4</sup> Flynn et al<sup>5</sup> developed a set of 5 predictor variables, including duration and pattern of symptoms, spinal mobility and hip range of motion, and patient attitudes, which identified a subgroup of back pain patients likely to benefit from spinal manipulation. A later study<sup>6</sup> refined these variables to just 2, namely, duration and pattern of symptoms, which were able to predict those patients most likely to improve after manipulation. In the first steps toward generating a clinical prediction rule, Tseng et al<sup>7</sup> were able to

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Paper submitted July 26, 2007; in revised form October 4, 2007; accepted October 4, 2007.

0161-4754/\$34.00

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doi:10.1016/j.jmpt.2008.02.007

identify a set of 6 variables that predicted neck pain patients most likely to respond to cervical spine manipulation.

Spinal manipulation, like most interventions, can be associated with adverse effects in which there is a transient worsening of the presenting complaint(s). For example, increased stiffness and soreness and headache are common in clinical practice.<sup>8-11</sup> It would therefore be clinically useful to predict not only those patients likely to respond to manipulative treatment, but also those likely to experience adverse effects. The aim of this study was therefore to develop prediction rules to help identify patients likely to either benefit or worsen from cervical spine manipulation. To do this, a large-scale, prospective cohort study was conducted to establish and document the incidence and nature of beneficial outcomes and/or adverse effects after neck manipulation treatments administered by chiropractors.

## METHODS

All registered chiropractors who were members of the British and Scottish Chiropractic Associations (1183 at the time) were invited to participate. Standardized forms recorded details on treatment and outcomes in patients 16 years and older receiving chiropractic treatment in which at least one cervical spine manipulation was administered. *Manipulation* was defined as a high-velocity/low-amplitude or mechanically assisted thrust to the cervical spine. Recordings, all of which were made by the treating chiropractor, occurred over a 6-week period on either 100 consecutive treatment consultations or consecutive treatment consultations to the end of this period, whichever was the sooner. The primary sampling units were the (a) treatment consultation and (b) follow-up period (up to 7 days after the consultation). Event rates are therefore reported for these units and not for individual patients.

Approval for the study was obtained from the University of Portsmouth Ethics Committee; in addition, a detailed opinion was received from the Multicentre Research Ethics Committee. All patients gave written informed consent for inclusion in the study.

### Predictor Variables

At the treatment consultation, details were recorded on the patients' sex, age, and presenting symptoms; the number and types of manipulative procedures; the areas of the cervical spine treated; and whether the patient had received a neck manipulation within the previous 4 weeks. The predictor variables were selected by clinician consensus through the process of a peer-review study before the main study.

### Outcome Variables

At the end of the treatment consultation, details were recorded on any immediate changes (improvement/worsen-

**Table 1.** Presenting symptoms at baseline (not mutually exclusive)

Presenting symptoms	n	%
Neck pain	15 559	54.0
Shoulder, arm pain	8690	30.2
Reduced neck, shoulder, arm movement, stiffness	17 793	61.8
Headache	3647	12.7
Face pain, numbness, tingling	900	3.1
Numbness, tingling upper limbs	2116	7.3
Upper, mid back pain	5245	18.2
Numbness, tingling lower limbs	860	3.0
Fainting, dizziness, light-headedness	1099	3.8
Ringing in ears, tinnitus	1040	3.6
Nausea, vomiting	647	2.2
Vision problems	700	2.4

Total number of treatment consultations is 28 807.

n, Number of treatment consultations.

ing) in presenting symptoms. On the return visit, up to 7 days later, patients were asked to indicate whether their condition, in global terms, was (a) "much better and a noticeable change that has made a real difference" or (b) "slightly better but no noticeable or worthwhile difference," or whether (c) "no change or worse." For the analysis of the results, descriptors *b* and *c* were collapsed into a "no global improvement" group.

### Data Analysis

A 2-pronged approach consisting of risk (odds ratios [ORs]) and comparison ( $\chi^2$  analysis) statistics was used to identify predictor variables of outcome. Simple (crude OR) logistic regression was used to identify the effects of each potential predictor variables on the 3 outcome groups. The latter was each dichotomized into (a) "immediate improvement" vs "no immediate improvement" in presenting symptoms, (b) "immediate worsening" vs no "immediate worsening" in presenting symptoms, and (c) "global improvement" vs "no global improvement"; 95% confidence intervals (CIs) were used to indicate the (im)precision of the estimates as population values. For each potential predictor variable, the crude OR was adjusted, using multiple logistic regression, for all other potential predictor variables in the model. The potential predictor variables were also tested for their distribution within each of the 3 outcome groups using  $\chi^2$  analysis.

Once the significant predictor variables were identified from the adjusted odds ratios ( $P < .05$ ) and from the  $\chi^2$  analysis ( $P < .10$ ), they were entered into stepwise multiple logistic regression analyses to construct prediction models for each of the outcome variables. A more liberal significance level was chosen for the comparison statistics to avoid excluding potential predictor variables. Statistical significance for the multiple logistic regression was set at  $P < .05$ .

For the predictor variables of presenting symptoms, accuracy analyses including sensitivity, specificity, and positive likelihood ratios (PLRs) were calculated for the prediction models based on the number of symptoms

**Table 2.** Predictors of immediate improvement using comparison ( $\chi^2$ ) and risk (crude and adjusted ORs) statistics

Factor	Predictor variables (independent)	Immediate improvement n (%)	No immediate improvement n (%)	$\chi^2$	P	OR crude	95% CI	OR adjusted <sup>a</sup>	95% CI
Sex	Female (17300)	12390 (71.6)	4910 (28.4)	—	—	1.00	—	1.00	—
	Male (11338)	7693 (67.9)	3645 (32.2)	46.4	<.001	0.84	0.79-0.88	0.87	0.82-0.93
Age	Age in years	—	—	10.13	<.001	0.99	0.99-1.00	1.00	0.99-1.003
Procedure	HVLA rot								
	No (14754)	10046 (68.1)	4708 (31.9)	—	—	1.00	—	1.00	—
	Yes (14053)	10148 (72.2)	3905 (27.8)	58.3	<.001	1.22	1.16-1.28	1.23	1.10-1.38
	HVLA lat flex								
	No (13986)	9590 (68.6)	4396 (31.4)	—	—	1.00	—	1.00	—
	Yes (14821)	10604 (71.6)	4217 (28.4)	30.4	<.001	1.15	1.10-1.21	1.26	1.12-1.41
	Mech manip device								
	No (25486)	18057 (70.9)	7429 (29.2)	—	—	1.00	—	1.00	—
	Yes (3321)	2137 (64.3)	1184 (35.7)	59.0	<.001	0.74	0.69-0.80	0.84	0.74-0.97
	Toggle								
No (28123)	19732 (70.2)	8391 (29.8)	—	—	1.00	—	1.00	—	
Yes (684)	462 (67.5)	222 (32.5)	2.18	=.14	0.89	0.75-1.04	0.97	0.77-1.22	
Area	Occiput to C2								
	No (14576)	10091 (69.2)	4485 (30.8)	—	—	1.00	—	1.00	—
	Yes (14231)	10103 (71.0)	4128 (29.0)	10.70	<.001	1.09	1.03-1.14	0.99	0.91-1.09
	C3 to C7								
No (7198)	4832 (67.1)	2366 (32.9)	—	—	1.00	—	1.00	—	
Yes (21609)	15362 (71.1)	6247 (28.9)	40.36	<.001	1.20	1.14-1.28	0.97	0.87-1.07	
Previous manipulation	No (13756)	9514 (69.2)	4242 (30.8)	—	—	1.00	—	1.00	—
	Yes (15051)	10680 (71.0)	4371 (29)	11.06	<.001	1.09	1.04-1.15	0.97	0.91-1.03
Frequency	Only 1 manipulation								
	No (18502)	13605 (73.5)	4897 (26.5)	—	—	1.00	—	1.00	—
Yes (10305)	6589 (63.9)	3716 (36.1)	288.7	<.001	0.64	0.61-0.67	0.97	0.90-1.05	
Presenting symptoms	Neck pain								
	No (13248)	7124 (53.8)	6124 (46.2)	—	—	1.00	—	1.00	—
	Yes (15559)	13070 (84.0)	2489 (16.0)	2905.08	<.001	4.51	4.27-4.77	3.78	3.53-4.06
	Shoulder, arm pain								
	No (20117)	12986 (64.6)	7131 (35.4)	—	—	1.00	—	1.00	—
	Yes (8690)	7208 (82.9)	1482 (17.1)	936.29	<.001	2.67	2.51-2.84	1.90	1.74-2.06
	Reduced neck, shoulder, arm movement, stiffness								
	No (11014)	4352 (39.5)	6662 (60.5)	—	—	1.00	—	1.00	—
	Yes (17793)	15842 (89.0)	1951 (11.0)	6646.26	<.001	12.43	11.70-13.21	13.87	12.94-14.86
	Headache								
	No (25160)	17241(68.5)	7919 (31.5)	—	—	1.00	—	1.00	—
	Yes (3647)	2953 (81.0)	694 (19)	228.64	<.001	1.95	1.79-2.13	2.53	2.22-2.88
	Face pain, numbness, tingling								
	No (27907)	19648 (70.4)	8259 (29.6)	—	—	1.00	—	1.00	—
	Yes (900)	546 (60.7)	354 (39.3)	38.99	<.001	0.65	0.57-0.77	0.49	0.38-0.63
	Numbness, tingling upper limbs								
	No (26691)	18672 (70.0)	8019 (30)	—	—	1.00	—	1.00	—
	Yes (2116)	1522 (71.9)	594 (28.1)	3.64	=.06	1.1	0.99-1.21	0.99	0.85-1.16
	Upper, mid back pain								
	No (23562)	15671 (66.5)	7891 (33.5)	—	—	1.00	—	1.00	—
Yes (5245)	4523 (86.2)	722 (13.8)	734.57	<.001	3.15	2.90-3.43	3.44	3.06-3.85	
Numbness, tingling lower limbs									
No (27947)	19682 (70.4)	8265 (29.6)	—	—	1.00	—	1.00	—	
Yes (860)	512 (59.5)	348 (40.5)	46.39	<.001	0.62	0.54-0.71	0.63	0.48-0.83	
Fainting, dizziness, light-headedness									
No (27708)	19482 (70.3)	8226 (29.7)	—	—	1.00	—	1.00	—	
Yes (1099)	712 (64.8)	387 (35.2)	15.33	<.001	0.78	0.69-0.88	0.84	0.66-1.07	

**Table 2** (continued)

Factor	Predictor variables (independent)	Immediate improvement n (%)	No immediate improvement n (%)	$\chi^2$	P	OR crude	95% CI	OR adjusted <sup>a</sup>	95% CI
Presenting symptoms	Ringing in ears, tinnitus					1.00		1.00	
	No (27 767)	19 554 (70.4)	8 213 (29.6)	–	–	–	–	–	–
	Yes (1040)	640 (61.5)	400 (38.5)	37.30	<.001	0.67	0.59-0.76	0.63	0.50-0.80
	Nausea, vomiting					1.00		1.00	
	No (28 160)	19 855 (70.5)	8 305 (29.5)	–	–	–	–	–	–
	Yes (647)	339 (52.4)	308 (47.6)	94.50	<.001	0.46	0.39-0.54	0.11	0.08-0.16
Vision problems	No (28 107)	19 813 (70.5)	8 294 (29.5)	–	–	1.00	–	1.00	–
	Yes (700)	381 (54.4)	319 (45.6)	81.03	<.001	0.50	0.43-0.58	0.25	0.18-0.35

HVLA, High-velocity/low-amplitude thrust manipulation; *lat flex*, lateral flexion; *rot*, rotation; *Mech manip device*, hand-operated mechanical manipulation device.

<sup>a</sup> Adjusted for all other variables.

**Table 3.** Predictors for immediate improvement after cervical spine manipulation (stepwise multiple logistical regression)

Predictor variables	P value	OR (adjusted <sup>a</sup> )	95% CI
Sex (male)	<.001	0.87	0.81-0.93
Presenting symptoms			
Neck pain	<.001	4.63	4.25-5.06
Shoulder, arm pain	<.001	2.36	2.12-2.58
Reduced neck, shoulder, arm movement, stiffness	<.001	16.33	15.05-17.72
Headache	<.001	3.05	2.66-3.50
Upper, mid back pain	<.001	4.08	3.61-4.61
Numbness, tingling lower limbs	<.001	0.61	0.47-0.81
Ringing in ears, tinnitus	<.001	0.68	0.54-0.85
Nausea, vomiting	<.001	0.08	0.05-0.11
Vision problems	<.001	0.21	0.15-0.29
Face pain, numbness, tingling	<.001	0.48	0.37-0.62
Type of manipulation			
Mech manip device	<.05	0.81	0.69-0.95
Area of manipulation			
Mid/lower	<.04	0.72	0.52-0.98
No. of presenting symptoms			
None or 1	<.001	1.58	1.41-1.77

<sup>a</sup> Adjusted for all other variables.

present. The PLR is calculated as “sensitivity/(1 – specificity)” and indicates how much a given prediction model can raise the probability of obtaining the outcome.<sup>12</sup> A PLR of 1 means that the posttest probability is the same as the pretest probability, PLRs of 1 to 2 alter probability to a small and rarely important degree, values between 2 and 5 generate small but sometimes important changes, and values between 5 and 10 generate moderate shifts; PLRs above 10 signify conclusive shifts from pretest to posttest probability.<sup>13</sup> In addition, nomograms<sup>14</sup> were plotted for each number of predictors (presenting symptoms) present to illustrate the effect of the PLRs in converting pre- to postprediction probabilities.

Statistical analyses were performed by using SPSS, version 15.0 (SPSS Inc, Chicago, Ill) and Confidence

**Table 4.** Number of treatment visits for immediate improvement in relation to presenting symptoms at each level of the prediction model

No. of predictor variables present	No. of treatment visits in improvement group	No. of treatment visits in no improvement group
5	517	295
4	1832	125
3	4581	454
2	6799	1117
1	6342	1767
0	123	4855

Interval Analysis, version 2.0 ([www.medschool.soton.ac.uk/cia/](http://www.medschool.soton.ac.uk/cia/)).

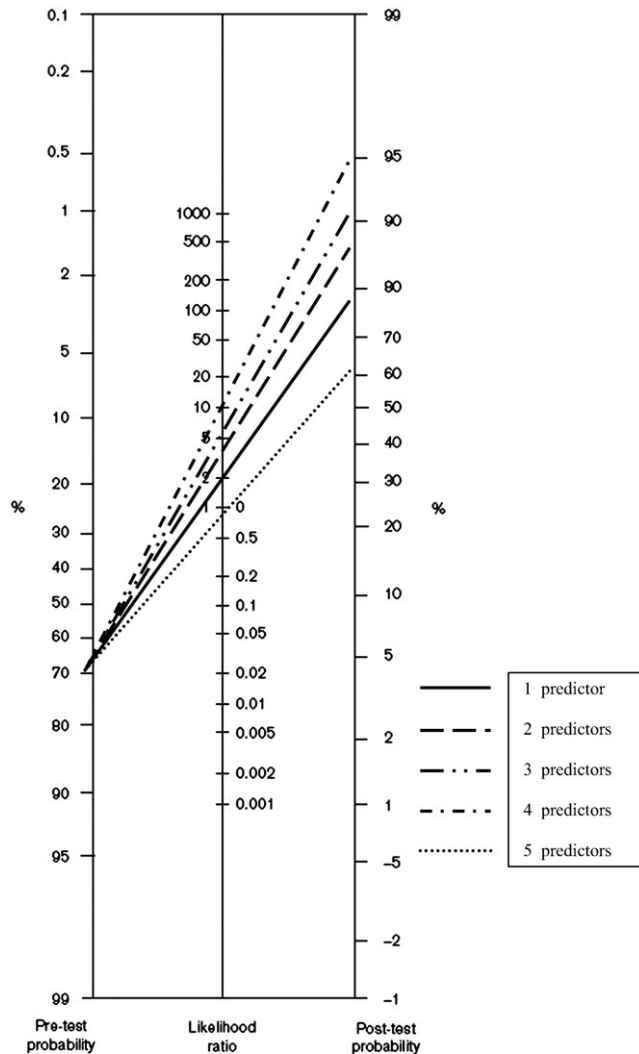
## RESULTS

### Sample Characteristics

Of the target population, 377 chiropractors (31.9%) took part in the study. The sample was made up of 28 807 treatment consultations, in which at least one cervical spine manipulation was administered, which represented 19 722 patients (age range, 16-100 years; mean (SD), 47.3 (14.01) years; ~60% female). A profile of the presenting complaints (not mutually exclusive) of these patients is shown in Table 1. As shown, most patients presented with pain or stiffness in the neck, shoulder, or arm region. From the 28 807 treatment consultations, data were collected on 13 873 follow-up treatment visits recording global improvement. The disparity between the number of treatment consultations and the number of follow-up visits is explained, in the main, by those follow-up visits that fell outside of the 6-week data collection period. The remainder, which was not explained in this way, represented 1.4% (403) of the treatment consultations.

### Immediate Improvement in Presenting Symptoms

An immediate improvement in presenting symptoms after cervical spine manipulation was reported in 20 083 (69.7%)



**Fig 1.** Nomogram of the prediction model for immediate improvement in presenting symptoms after neck manipulation.

treatment consultations. There were 14 variables identified as significant predictors of immediate improvement in presenting symptoms (Table 2), which were subsequently entered into a stepwise multiple logistic regression analysis (Table 3). From these, “neck pain,” “shoulder, arm pain,” “reduced neck, shoulder, arm movement, stiffness,” “headache,” “upper, mid back pain,” and “none or one presenting symptom” emerged in the final prediction model as significant predictors for an immediate improvement in presenting symptoms after cervical spine manipulation.

To assess the relevance of presenting symptoms within the context of a clinical prediction model, for all of the significant predictor variables falling under the category of presenting symptoms, an accuracy analysis for each level (number of variables) of the prediction model was performed. Table 4 shows the number of treatment consultations in the immediate improvement outcome

**Table 5.** Accuracy analyses (with 95% CI) for each level of the prediction model in relation to presenting symptoms

No. of predictor variables present	Sensitivity	Specificity	PLR	Probability of immediate improvement (%)
1	0.31 (0.31-0.32)	0.80 (0.79-0.80)	1.53 (1.46-1.60)	75
2	0.34 (0.33-0.34)	0.87 (0.86-0.88)	2.60 (2.45-2.75)	85
3	0.23 (0.22-0.23)	0.95 (0.94-0.95)	4.30 (3.92-4.72)	90
4	0.09 (0.09-0.10)	0.99 (0.98-0.99)	6.25 (5.22-7.48)	94
5	0.03 (0.02-0.03)	0.97 (0.96-0.97)	0.75 (0.65-0.86)	60

The probability of immediate improvement is calculated using the PLR and assumes a pretest probability of improvement of ~70%.

group in relation to the number of presenting symptoms. The PLR and the postprediction or posttest probability were calculated for each level of the model (Table 5). As shown in Figure 1, the presence of any 4 of these predictors raised the probability for an immediate improvement in presenting symptoms after treatment from 70% to ~95%.

#### Immediate Worsening in Presenting Symptoms

A worsening of presenting symptoms was reported in 1269 (4.4%) treatment consultations. In this case, 18 variables were identified as significant predictors of immediate worsening (Table 6), which were then entered into a stepwise multiple logistic regression analysis (Table 7). From these, “neck pain,” “shoulder, arm pain,” “headache,” “numbness, tingling upper limbs,” “upper, mid back pain,” and “fainting, dizziness, light-headedness” emerged in the final prediction model as significant presenting symptom predictors for immediate worsening after cervical spine manipulation.

Table 8 shows the number of treatment consultations in the immediate worsening outcome group in relation to the number of presenting symptoms. The results of the accuracy analyses including sensitivity, specificity, PLR, and post-prediction probability of immediate worsening for each level of the model are shown in Table 9. As shown in Figure 2, the presence of any 4 of these predictors raised the posttreatment probability for an immediate worsening in presenting symptoms from 4.4% to ~12%.

#### Global Improvement

Of the 13 873 follow-up treatment visits, global improvement was recorded in 7775 (56.0%). Comparison and risk statistics for all potential predictor variables for global improvement are presented in Table 10. Stepwise multiple logistic regression analysis showed that only “neck pain” and the use of “toggle” manipulation significantly predicted global improvement (Table 11). Because only 2 variables

**Table 6.** Predictors of immediate worsening using comparison ( $\chi^2$ ) and risk (crude and adjusted ORs) statistics

Factor	Predictor variables (independent)	Immediate worsening n (%)	No immediate worsening n (%)	$\chi^2$	P	OR crude	95% CI	OR adjusted <sup>a</sup>	95% CI
Sex	Female (17300)	834 (4.8)	16466 (95.2)	–	–	1.00	–	1.00	–
	Male (11338)	435 (3.8)	10903 (96.2)	15.60	<.001	0.79	0.70-0.89	0.87	0.77-0.99
Age	Age in years	–	–	11.58	<.001	0.99	0.99-1.00	1.01	1.00-1.01
Procedure	HVLA rot								
	No (14754)	676 (4.6)	14078 (95.4)	–	–	1.00	–	1.00	–
	Yes (14053)	599 (4.3)	13454 (95.7)	1.74	=.19	0.93	0.83-1.04	1.03	0.86-1.23
	HVLA lat flex								
	No (13986)	545 (3.9)	13441 (96.1)	–	–	1.00	–	1.00	–
	Yes (14821)	730 (4.9)	14091 (95.1)	17.92	<.001	1.28	1.14-1.43	1.28	1.07-1.53
	Mech manip device								
	No (25486)	1136 (4.5)	24350 (95.5)	–	–	1.00	–	1.00	–
	Yes (3321)	139 (4.2)	3182 (95.8)	0.52	=.47	0.94	0.78-1.12	1.03	0.81-1.30
	Toggle								
	No (28123)	1251 (4.4)	26872 (95.6)	–	–	1.00	–	1.00	–
	Yes (684)	24 (3.5)	660 (96.5)	1.39	=.24	0.78	0.52-1.18	1.02	0.66-1.58
Area	Occiput to C2								
	No (14576)	671 (4.6)	13905 (95.4)	–	–	1.00	–	1.00	–
	Yes (14231)	604 (4.2)	13627 (95.8)	2.20	=.14	0.92	0.82-1.03	0.93	0.80-1.08
	C3 to C7								
	No (7198)	259 (3.6)	6939 (96.4)	–	–	1.00	–	1.00	–
	Yes (21609)	1016 (4.7)	20593 (95.3)	15.45	<.001	1.32	1.15-1.52	1.16	0.97-1.39
Previous manipulation	No (13756)	564 (4.1)	13192 (95.9)	–	–	1.00	–	1.00	–
	Yes (15051)	711 (4.7)	14340 (95.3)	6.60	<.05	1.16	1.04-1.30	1.08	0.96-1.21
Frequency	Only 1 manipulation								
	No (18502)	860 (4.6)	17642 (95.4)	–	–	1.00	–	1.00	–
	Yes (10305)	415 (4.0)	9890 (96.0)	6.0	<.05	0.86	0.76-0.97	1.06	0.92-1.21
Presenting symptoms	Neck pain								
	No (13248)	307 (2.3)	12941 (97.7)	–	–	1.00	–	1.00	–
	Yes (15559)	968 (6.2)	14591 (93.8)	238.40	<.001	2.80	2.45-3.19	2.10	1.82-2.42
	Shoulder, arm pain								
	No (20117)	645 (3.2)	19472 (96.8)	–	–	1.00	–	1.00	–
	Yes (8690)	630 (7.2)	8060 (92.8)	222.47	<.001	2.40	2.11-2.64	1.57	1.39-1.78
	Reduced neck, shoulder, arm movement, stiffness								
	No (11014)	391 (3.6)	10623 (96.4)	–	–	1.00	–	1.00	–
	Yes (17793)	884 (5.0)	16909 (95.0)	32.10	<.001	1.42	1.26-1.60	1.02	0.89-1.16
	Headache								
	No (25160)	1008 (4.0)	24152 (96.0)	–	–	1.00	–	1.00	–
	Yes (3647)	267 (7.3)	3380 (92.7)	80.22	<.001	1.89	1.65-2.18	1.35	1.15-1.59
	Face pain, numbness, tingling								
	No (27907)	1212 (4.3)	26695 (95.7)	–	–	1.00	–	1.00	–
	Yes (900)	63 (7.0)	837 (93.0)	14.25	<.001	1.66	1.28-2.16	0.80	0.54-1.19
	Numbness, tingling upper limbs								
	No (26691)	1058 (4.0)	25633 (96.0)	–	–	1.00	–	1.00	–
	Yes (2116)	217 (10.3)	1899 (89.7)	169.46	<.001	2.77	2.38-3.23	2.12	1.77-2.53
	Upper, mid back pain								
	No (23562)	862 (3.7)	–	–	–	1.00	–	1.00	–
	Yes (5245)	413 (7.9)	–	171.75	<.001	2.25	1.99-2.54	1.63	1.42-1.86
	Numbness, tingling lower limbs								
	No (27947)	1220 (4.4)	26727 (95.4)	–	–	1.00	–	1.00	–
	Yes (860)	55 (6.4)	805 (93.6)	8.02	<.005	1.50	1.13-1.98	0.70	0.45-1.08
	Fainting, dizziness, light-headedness								
	No (27708)	1143 (4.1)	26565 (95.9)	–	–	1.00	–	1.00	–
	Yes (1099)	132 (12.0)	967 (88.0)	139.98	<.001	3.17	2.62-3.84	3.60	2.78-4.56
	Ringings in ears, tinnitus								
	No (27767)	1215 (4.4)	26552 (95.6)	–	–	1.00	–	1.00	–
	Yes (1040)	60 (5.8)	980 (94.2)	4.60	<.05	1.34	1.03-1.75	0.67	0.45-1.01
	Nausea, vomiting								
	No (28160)	1235 (4.4)	26925 (95.6)	–	–	1.00	–	1.00	–
	Yes (647)	40 (6.2)	607 (93.8)	4.78	<.05	1.44	1.04-1.99	0.19	0.10-0.35

(continued on next page)

**Table 6** (continued)

Factor	Predictor variables (independent)	Immediate worsening n (%)	No immediate worsening n (%)	$\chi^2$	<i>P</i>	OR crude	95% CI	OR adjusted <sup>a</sup>	95% CI
Presenting symptoms	Vision problems								
	No (28 107)	1217 (4.3)	26 890 (95.7)	–	–	1.00	–	1.00	–
	Yes (700)	58 (8.3)	642 (91.7)	24.3	<.001	2.00	1.52-2.63	1.25	0.80-1.98

<sup>a</sup> Adjusted for all other variables.

**Table 7.** Predictors for immediate worsening after cervical spine manipulation (stepwise multiple logistical regression)

Predictor variables	<i>P</i> value	OR (adjusted <sup>a</sup> )	95% CI
Sex (male)	<.04	0.87	0.81-0.93
Presenting symptoms			
Neck pain	<.001	1.53	1.30-1.80
Shoulder, arm pain	<.001	1.35	1.20-1.54
Reduced neck, shoulder, arm movement, stiffness	<.006	0.82	0.72-0.95
Headache	<.008	1.24	1.06-1.46
Numbness, tingling upper limbs	<.001	1.96	1.65-2.34
Upper, mid back pain	<.001	1.51	1.32-1.72
Numbness, tingling lower limbs	<.12	0.71	0.47-1.09
ringing in ears, tinnitus	<.02	0.62	0.47-0.92
Nausea, vomiting	<.001	0.25	0.14-0.45
Vision problems	<.29	1.27	0.82-1.97
Face pain, numbness, tingling	<.35	0.83	0.57-1.22
Fainting, dizziness, light-headedness	<.001	3.22	2.52-4.11
No. of presenting symptoms			
None or 1	<.001	0.46	0.37-0.57
Type of manipulation			
HVLA lat flex	<.001	1.27	1.12-1.43
Area of manipulation			
Mid/lower	<.02	1.20	1.03-1.39
No. of manipulations			
Only 1	<.33	1.07	0.94-1.22
Manipulation in previous 4 wk	<.19	1.08	0.96-1.21

<sup>a</sup> Adjusted for all other variables.

(including one that was not a presenting symptom) were identified, both were included in the subsequent analyses.

Table 12 shows the data for the number of treatment visits in the global improvement outcome group, and Table 13 shows the PLR and the posttest probability for each level of the model. As shown in Figure 3, the presence of any one of these predictors had the effect of raising the probability of reporting an overall improvement very slightly from 56% to 60%.

## DISCUSSION

This was a large-scale study investigating potential predictors of response to cervical spine manipulation.

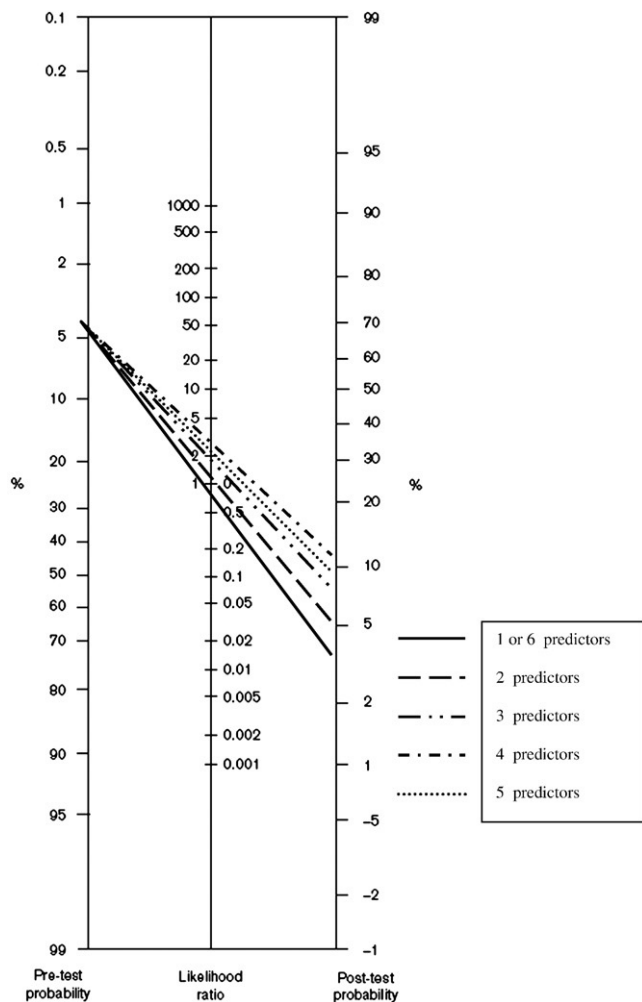
**Table 8.** Number of treatment visits for immediate worsening in relation to presenting symptoms at each level of the prediction model

No. of predictor variables present	No. of treatment visits in worsening group	No. of treatment visits in no worsening group
6	21	441
5	18	120
4	103	621
3	260	2360
2	401	6051
1	417	8817
0	55	9122

Although most of the patients in this study presented with either neck pain or reduced neck movement, these were not the only inclusion criteria. Hence, patients with other presenting symptoms for which cervical spine manipulation was indicated were included. Patients in whom a pathological cause is most usually absent are notorious for a mixed response to treatment; some respond well, whereas others do not. Being able to predict in advance of treatment those who will likely improve and those who, in the short term at least, may worsen is an extremely attractive proposition for clinicians in their management of patients.

The study by Tseng et al<sup>7</sup> appears to be the only one to date that has established clinical prediction models for immediate responders to neck manipulation. These investigators identified 6 variables that significantly predicted an immediate response, including self-reported measures and examination findings. They also established that the presence of 4 or more of these predictors increased the probability of success with manipulation from 60% to 89%. For the present study, a similar methodological approach was adopted to establish prediction models based on patient demographics, treatment, and presenting symptoms.

The most robust predictive model was identified for immediate improvement in presenting symptoms after treatment. In the final model, the presenting symptoms of “neck pain,” “shoulder, arm pain,” “headache,” and “upper, mid back pain” all significantly predicted an immediate



**Fig 2.** Nomogram of the prediction model for immediate worsening in presenting symptoms after neck manipulation.

improvement in presenting symptoms after cervical spine manipulation. The strongest predictor for immediate improvement after manipulation was the presenting symptom of “stiffness.”

The preprediction probability of immediate improvement in presenting symptoms after treatment was 70%. In other words, randomly manipulating individuals in this sample, without any attempt at prediction, may result in success in about 70% of the time. Our findings suggest that if at least 2 of the identified predictors are present, there is an 85% probability of achieving immediate improvement in presenting symptoms after manipulation. With 4 predictor variables present, the probability of achieving immediate improvement is raised to 95%. Paradoxically, with all 5 predictor variables in the model, the postprediction probability fell to 60%, that is, to a level lower than that of the preprediction probability for improvement. The most likely reason for this is that the model was constructed purely on the basis of an additive

**Table 9.** Accuracy analyses (with 95% CI) for each level of the prediction model in relation to presenting symptoms

No. of predictor variables present	Sensitivity	Specificity	PLR	Probability of immediate worsening (%)
1	0.33 (0.30-0.35)	0.68 (0.67-0.69)	1.02 (0.94-1.11)	4
2	0.32 (0.29-0.34)	0.79 (0.77-0.79)	1.43 (1.32-1.56)	5
3	0.20 (0.18-0.23)	0.91 (0.91-0.92)	2.38 (2.12-2.67)	8
4	0.08 (0.07-0.10)	0.98 (0.98-0.98)	3.58 (2.93-4.38)	13
5	0.01 (0.01-0.02)	1.00 (0.99-1.00)	3.24 (1.98-5.23)	10
6	0.02 (0.01-0.03)	0.98 (0.98-0.99)	1.03 (0.67-1.59)	4

The probability of immediate worsening is calculated using the PLR and assumes a pretest probability of worsening of 4.4%.

format and that, in reality, a linear relationship does not apply. It is quite possible that there are inverse relationships in the interactions between some of the predictor variables and that, by the nature of their combination, they actually lower the postprediction probability for achieving immediate improvement. In clinical practice, the presence of multiple symptoms is generally regarded to be a nonfavorable prognostic indicator. As such, it is conceivable that there could be a “critical” number of presenting symptoms or a combination of certain symptoms that, once reached or present, results in a lowering of the probability for improvement.

Using a similar analytic model, 8 variables were found to significantly predict immediate worsening in presenting symptoms after manipulation. Of these, “fainting, dizziness, light-headedness” and “numbness, tingling upper limbs” were the strongest. The preprediction probability of immediate worsening was 4.4%; and with 4 predictors present, this was raised to 12%. As was the case with the model for immediate improvement, adding more than 4 predictors resulted in a lowering of the postprediction probability. Again, the most likely explanation lies in the relationships in the interactions between variables.

When considering immediate response to neck manipulation, it is apparent that some of the same predictors can either predict improvement or worsening. This was the case for “neck pain,” “shoulder, arm pain,” “headache,” and “upper, mid back pain.” Although, for both of the outcomes, the predictor variables had achieved statistical significance, the ORs were much more favorable in terms of the prediction of immediate improvement and, as such, would tend to indicate stronger clinical significance. Furthermore, this situation reflects clinical practice, where there is often an absence of well-defined



**Table 10.** Predictors of global improvement using comparison ( $\chi^2$ ) and risk (crude and adjusted odds ratios) statistics

Factor	Predictor variables (independent)	Global improvement n (%)	No global improvement n (%)	$\chi^2$	P	OR crude	95% CI	OR adjusted <sup>a</sup>	95% CI
Sex	Female (8500)	4758 (56.0)	3742 (44.0)	–	–	1.00	–	1.00	–
	Male (5469)	3021 (55.2)	2448 (44.8)	0.734	=.39	0.97	0.91-1.04	0.94	0.88-1.01
Age	Age in years	–	–	44.53	<.001	0.99	0.99-0.994	0.99	0.99-1.00
Procedure	HVLA rot								
	No (7092)	3899 (55.0)	3193 (45.0)	–	–	1.00	–	1.00	–
	Yes (6927)	3906 (56.4)	3021(43.6)	2.82	=.09	1.06	0.99-1.13	0.99	0.89-1.11
	HVLA lat flex								
	No (6879)	3756 (54.6)	3123 (45.4)	–	–	1.00	–	–	–
	Yes (7140)	4049 (56.7)	3091 (43.3)	6.31	<.05	1.09	1.02-1.16	1.04	0.93-1.16
	Mech manip device								
	No (12258)	6959 (56.8)	5299 (43.2)	–	–	1.00	–	1.00	–
	Yes (1761)	846 (48.0)	915 (52.0)	47.23	<.001	0.70	0.64-0.78	0.75	0.65-0.87
	Toggle								
	No (13683)	7595 (55.5)	6088 (44.5)	–	–	1.00	–	1.00	–
	Yes (336)	210 (62.5)	126 (37.5)	6.46	<.05	1.34	1.07-1.67	1.36	1.10-1.75
Area	Occiput to C2								
	No (6997)	3901 (55.8)	3096 (44.2)	–	–	1.00	–	1.00	–
	Yes (7022)	3904 (55.6)	3118 (44.4)	0.03	=.85	0.99	0.93-1.06	0.95	0.86-1.04
	C3 to C7								
	No (3494)	1951 (55.8)	1543 (44.2)	–	–	1.00	–	1.00	–
	Yes (10525)	5854 (55.6)	4671 (44.4)	0.05	=.82	0.99	0.92-1.07	0.98	0.88-1.09
Previous manipulation	No (3943)	2242 (56.9)	1701 (43.1)	–	–	1.00	–	1.00	–
	Yes (9186)	5042 (54.9)	4144 (45.1)	4.35	<.05	0.92	0.86-0.96	0.92	0.85-0.99
Frequency	Only 1 manipulation								
	No (8972)	5048 (56.3)	3924 (43.7)	–	–	1.00	–	1.00	–
	Yes (5047)	2757 (54.6)	2290 (45.4)	3.51	=.06	0.94	0.87-1.00	0.90	0.83-0.98
Presenting symptoms	Neck pain								
	No (5294)	2898 (54.7)	2396 (55.3)	–	–	1.00	–	1.00	–
	Yes (8725)	4907 (56.2)	3818 (43.8)	3.00	=.08	1.06	0.99-1.14	1.14	1.05-1.23
	Shoulder, arm pain								
	No (8951)	5110 (57.1)	3841 (42.9)	–	–	1.00	–	1.00	–
	Yes (5068)	2695 (53.2)	2373 (46.8)	20.05	<.001	0.85	0.80-0.92	0.86	0.80-0.93
	Reduced neck, shoulder, arm movement, stiffness								
	No (4881)	2675 (54.8)	2206 (45.2)	–	–	1.00	–	1.00	–
	Yes (9138)	5130 (56.1)	4008 (43.9)	2.30	=.13	1.06	0.98-1.13	1.08	1.00-1.17
	Headache								
	No (12032)	6753 (56.1)	5279 (43.9)	–	–	1.00	–	1.00	–
	Yes (1987)	1052 (52.9)	935 (47.1)	6.99	<.05	0.88	0.80-0.97	0.93	0.83-1.04
	Face pain, numbness, tingling								
	No (13567)	7605 (56.1)	5962 (43.9)	–	–	1.00	–	1.00	–
	Yes (452)	200 (44.2)	252 (55.8)	24.30	<.001	0.62	0.52-0.75	0.95	0.74-1.23
	Numbness, tingling upper limbs								
	No (12770)	7196 (56.4)	5574 (43.6)	–	–	1.00	–	1.00	–
	Yes (1249)	609 (48.8)	640 (51.2)	26.42	<.001	0.74	0.66-0.83	0.89	0.78-1.02
	Upper, mid back pain								
	No (11192)	6293 (56.3)	4899 (43.7)	–	–	1.00	–	1.00	–
	Yes (2827)	1512 (53.5)	1315 (46.5)	6.88	<.05	0.90	0.83-0.97	0.94	0.85-1.03
	Numbness, tingling lower limbs								
	No (13597)	7627 (56.1)	5970 (43.9)	–	–	1.00	–	1.00	–
	Yes (422)	178 (42.2)	244 (57.8)	31.35	<.001	0.57	0.47-0.70	0.87	0.67-1.13
	Fainting, dizziness, light-headedness								
	No (13420)	7530 (56.1)	5890 (43.9)	–	–	1.00	–	1.00	–
	Yes (599)	275 (45.9)	324 (54.1)	23.88	<.001	0.66	0.56-0.78	0.96	0.78-1.20

**Table 10** (continued)

Factor	Predictor variables (independent)	Global improvement n (%)	No global improvement n (%)	$\chi^2$	P	OR crude	95% CI	OR adjusted <sup>a</sup>	95% CI	
Presenting symptoms	Ringing in ears, tinnitus	No (13 558)	5944 (43.8)	–	–	1.00	–	1.00	–	
		Yes (461)	191(41.4)	270 (58.6)	38.16	<.001	0.55	0.46-0.67	0.81	0.63-1.03
	Nausea, vomiting	No (13 697)	7680 (56.1)	6017 (43.9)	–	–	1.00	–	1.00	–
		Yes (322)	125 (38.8)	197 (61.2)	36.53	<.001	0.50	0.40-0.62	0.79	0.56-1.11
	Vision problems	No (13 675)	7666 (56.1)	6009 (43.9)	–	–	1.00	–	1.00	–
		Yes (344)	139 (40.4)	205 (59.6)	32.30	<.001	0.53	0.43-0.66	0.95	0.69-1.31

<sup>a</sup> Adjusted for all other variables.

**Table 11.** Predictors for global improvement after cervical spine manipulation (stepwise multiple logistical regression)

Predictor variables	P value	OR (adjusted <sup>a</sup> )	95% CI
Age (y)	<.001	0.99	0.99-0.97
Presenting symptoms			
Neck pain	<.05	1.12	1.00-1.25
Shoulder, arm pain	<.005	0.86	0.78-0.96
Type of manipulation			
Mech manip device	<.005	0.76	0.63-0.92
Toggle	<.05	1.37	1.04-1.80
No. of manipulations			
Only 1	<.05	0.92	0.85-0.99
Manipulation in previous 4 wk	<.05	0.92	0.85-0.99

<sup>a</sup> Adjusted for all other variables

borders and where the same symptoms can bring a different meaning to a clinical situation and must be interpreted in view of the complexity of the clinical presentation. For example, a combination of neck pain together with upper limb symptoms is likely to indicate a different prognosis when compared with neck pain combined with headache.

These results must be considered in context of 2 other studies that used multivariate analysis and effect estimates in the form of ORs and CIs for the prediction of adverse effects related to neck manipulation. The study by Cagnie et al<sup>11</sup> established headache as the most common postmanipulative reaction (in 19.8% of 280 patients) and, after multivariate analysis, concluded that upper cervical manipulation, use of medication, female sex, and age were all significant predictors of headache after spinal manipulation. In the University of California, Los Angeles, Neck Pain Study, Hurwitz et al<sup>9</sup> reported a number of predictors for adverse reactions after manipulation, including those of neck pain, stiffness/soreness, radiating pain/discomfort, tiredness/fatigue, headache, and neurologic symptoms (this category included among others symptoms of dizziness, nausea and vomiting, impaired vision, tinnitus,

**Table 12.** Number of treatment visits for global improvement at each level of the prediction model

No. of predictor variables present	No. of treatment visits in improvement group	No. of treatment visits in no improvement group
2	2880	2436
1	4925	3778

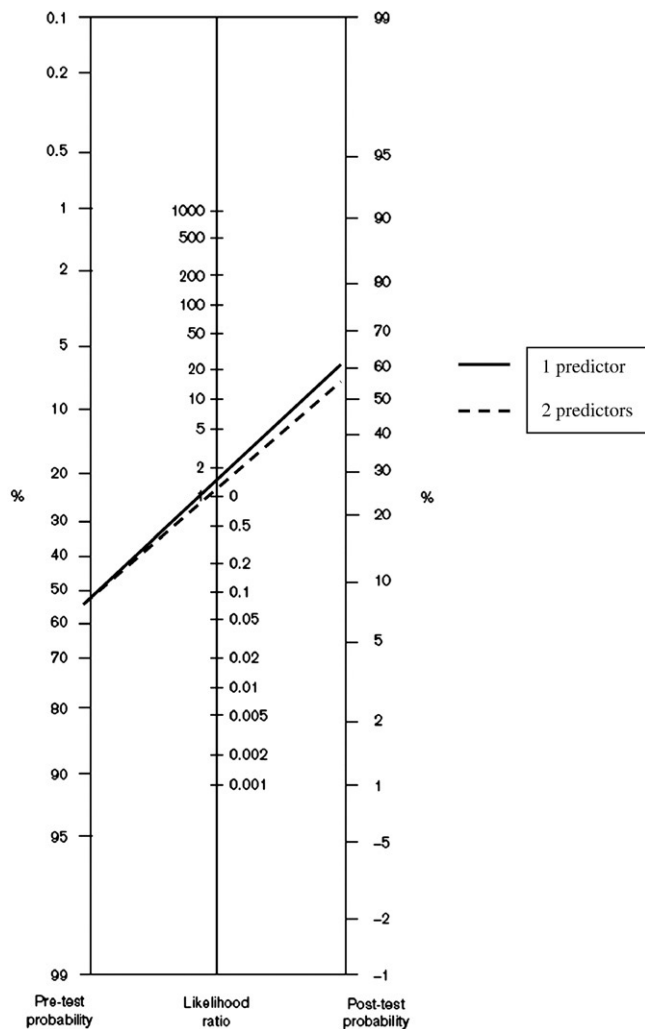
and lower limb symptoms). Their reported risks for these symptoms are not dissimilar to the ones obtained in the present study.

Finally, this study attempted to predict global improvement based on the data available from 13 873 follow-up treatments. Only the variables of “neck pain” and “toggle manipulation” were combined to significantly predict global improvement. However, in the accuracy analyses for these 2 predictors, the PLRs were approximately 1.0; and as such, it was not possible to identify any predictors for global improvement after cervical spine manipulation.

This study had a number of limitations. Despite being a prospective study with large numbers of data, these data were collected in routine clinical practices throughout the United Kingdom and as such are liable to issues of accuracy, reporting bias by the chiropractors and patients, and selection (of patient) bias. Patients participating in this study may also have been treated concurrently by other health care professionals. We relied on chiropractors recruiting treatment consultations in a consecutive manner. As the chiropractors were not blinded to the purpose, any deviation from this protocol may have introduced further bias.

## CONCLUSIONS

This study is the first attempt to identify variables that can predict immediate outcomes in terms of improvement and worsening of presenting symptoms, and global



**Fig 3.** Nomogram of the prediction model for global improvement (after the follow-up period) after neck manipulation.

improvement, after cervical spine manipulation. From the findings, it was possible to identify some predictors of immediate improvement in presenting symptoms after cervical spine manipulation. Patients presenting with symptoms of “reduced neck, shoulder, arm movement, stiffness,” “neck pain,” “upper, mid back pain,” “headache,” “shoulder, arm pain,” and/or “none or one presenting symptom only” are likely to report immediate improvement in these symptoms after treatment. Patients presenting with any 4 of these symptoms were shown to have the highest probability of immediate improvement. This finding may enhance clinical decision making for selecting cervical manipulation in the treatment of patients with one or more of these complaints. Although it was possible to identify a number of predictor variables for immediate worsening in presenting symptoms and

**Table 13.** Accuracy analyses (with 95% CI) for each level of the prediction model

No. of predictor variables present	Sensitivity	Specificity	PLR	Probability of global improvement (%)
1	0.63 (0.62-0.64)	0.39 (0.38-0.40)	1.04 (1.01-1.07)	60
2	0.37 (0.36-0.38)	0.61 (0.60-0.62)	0.94 (0.90-0.98)	55

The probability of global improvement is calculated using the PLR and assumes a pretest probability of improvement of 55.7%.

global improvement after cervical spine manipulation, these failed to provide a robust predictive model for clinical application.

### Practical Applications

- Predicting responses to treatment may aid in clinical decision making.
- Predictors can be obtained from patient presenting symptoms.
- Robust predictors could be identified for immediate improvement after neck manipulation.
- Patients presenting with symptoms of “reduced neck, shoulder, arm movement, stiffness,” “neck pain,” “upper, mid back pain,” “headache,” “shoulder, arm pain,” and/or “none or one presenting symptom only” are likely to report immediate improvement after treatment.
- Patients presenting with any 4 of these symptoms in the study had the highest probability of immediate improvement.
- These findings may enhance clinical decision making for selecting cervical manipulation in the treatment of patients with one or more of these complaints.

### ACKNOWLEDGMENT

The authors wish to thank Dr Sharon Docherty for her expert help in the administration of the study and compilation of the databases.

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