Reproducibility of the University of Toronto Self-administered Questionnaire Used to Assess Environmental Sensitivity

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Environmental sensitivity patients report symptoms provoked by low-level exposure to a wide range of substances. Features of published case definitions include nature of onset, chronicity, symptom provocation by multiple substances, symptom provocation by an escalating number of exposures, involvement of multiple body systems including the nervous system, provocation by unrelated substances, and addictive behaviors. This study assessed the reproducibility of a Canadian self-administered questionnaire, the University of Toronto Health Survey, designed to determine the prevalence of the features described in these case definitions. A total of 191 eligible respondents aged 16–70 years who attended several types of medical practices in 1994 were invited to complete a second questionnaire 5–7 months after the first; 134 (70.2%) complied. Total agreement on whether patients satisfied each of seven case definitions ranged from 80% to 90%. After adjustment for chance, major agreement was observed for three of the seven case definitions (kappa = 0.69, 0.68, and 0.78). The survey achieved good reproducibility regarding self-report of symptoms described in published case definitions of environmental sensitivity. *Am J Epidemiol* 2000;151:1216–22.

environmental illness; multiple chemical sensitivity; questionnaires; reproducibility of results; self administration; sensitivity and specificity; test reliability

Environmental sensitivity or multiple chemical sensitivity patients report symptoms associated with low-level exposures to a variety of substances (1–3). As of 1993, six case definitions had been proposed (4–9) that identified a number of symptoms and recognized the link between symptoms and low-level exposures. On the basis of these six definitions, we developed a Canadian questionnaire, the University of Toronto Health Survey (UTHS), to evaluate symptoms and additional features that had been described (G. E. McKeown-Eyssen et al., University of Toronto, manuscripts in preparation). After the reproducibility study had been conducted, a seventh definition, the 1999 consensus on multiple chemical sensitivity, was published (10). This paper evaluated the reproducibility of the UTHS with respect to all seven definitions.

MATERIALS AND METHODS

Questionnaire

The UTHS is a self-administered questionnaire in which respondents were asked to report general health and demographic characteristics. They were also asked which of 171 symptoms they had had in the previous 12 months, which symptoms were linked to exposures, and which of a list of exposures provoked symptoms. "Linkage" meant not only that exposures caused symptoms but also that avoiding an exposure relieved symptoms. Respondents also reported on the additional features described in seven published case definitions of environmental sensitivity (table 1). However, the questionnaire could not address features requiring physical examination (4, 8), use of diagnostic tests (4, 6, 10), exposure to substances in a controlled environment to observe symptom provocation in blinded patients (7, 8), or elicitation of symptoms after demonstrable exposures (6, 10). In the absence of any defined criteria for unrelatedness, the feature "provocation by unrelated substances" (7, 9, 10) also could not be addressed.

Reproducibility

Reproducibility of the questionnaire was assessed by comparing responses from people who completed it on

TABLE 1. Features* included in seven published case definitions of environmental sensitivity

Definitional feature	Case definition (reference no.)						
	Thomson et al. (4)	National Research Council (5)	Cullen (6)	Ashford and Miller (7)	Randolph (8)	Nethercott et al. (9)	1999 Consensus (10)
Symptoms linked to low-level exposure	Required	Required	Required	Required	Required	Required	Required
Multisystem	Required	Not required	Required	Not required	Not required		Required
Nervous system symptoms	Discussed				Discussed		
Chronic condition	Required				Not required	Required	Required
Acquired in response to an event		Not required	Required	Not required	Not required		
Spreading of incitants					Discussed		
Addictive responses							
Provocation by unrelated substances†	Discussed		Required		Discussed	Required	Required
Varying morbidity†	Required				Discussed		

* For each case definition, features are classified according to whether they were specifically required to identify a case, were specifically not required, were discussed but left optional, or were not mentioned.

† These features were included in the University of Toronto Health Survey but were not used in analysis because their meanings were not specified clearly by the authors.

two different occasions. Participants in the reproducibility study were randomly selected from more than 2,500 persons who in 1995 responded to the initial circulation of the UTHS in the greater metropolitan Toronto area. Within 5–7 months of returning the first questionnaire (Q1), 200 respondents were randomly selected to receive the questionnaire a second time (Q2) and were asked to report symptoms for the same 12-month period covered in their initial questionnaire.

Nine persons were excluded: five returned incomplete initial questionnaires, one had refused consent for follow-up contact after the initial questionnaire, one was not fluent in English, one was ineligible because the original questionnaire had been completed by the wrong person in the household, and one self-declared ineligibility for the study. A total of 134 people, 70.2 percent of the 191 people who received the second questionnaire, responded after a reminder card, a telephone call, and, when necessary, a second mailing.

Responders to Q2 were on average 6 years older than nonresponders ($p = 0.002$). In addition, responders included a higher percentage of women, were slightly more likely to report being married or living in a common-law relationship, were less likely to have been born in Canada, and were more likely to have a postsecondary education or a household income of $60,000 or more (table 2), although none of these differences reached statistical significance. Similar proportions of responders and nonresponders were currently employed and described themselves as professionals or high-level managers (table 2).

Analysis

Frequency distributions, means, and standard deviations were used to describe responses to the two sets of

TABLE 2. Characteristics† of responders and nonresponders to the reproducibility study of the University of Toronto Health Survey questionnaire, Ontario, Canada, 1995–1996

Characteristic	Responders ($n = 134$)	Nonresponders ($n = 57$)
Average age (years)	43.1* (12.5)‡	37.3 (10.6)‡
Female	72.4	64.9
Married/common-law	72.4	68.4
Born in Canada	60.4	64.9
Postsecondary education	69.4	59.6
Household income: ≥$60,000	43.3	36.8
Currently employed	69.4	66.7
Professional or high-level manager	30.6	31.6

* $p = 0.002$.
† All characteristics except age are expressed as percentages.
‡ Number in parentheses, standard deviation.

questionnaires. Agreement was assessed in terms of the total agreement observed and of agreement adjusted for chance by using the kappa statistic (11). Reproducibility was determined for each of the seven case definitions, for all respondents, and by gender and age.

First, Q1 and Q2 were compared regarding the number of symptoms reported, the number of body systems involved, and whether symptoms were associated with exposure. To assess the reproducibility of the questionnaire with respect to body system involvement, Q1 and Q2 were analyzed separately to determine which of the 13 body systems were involved for each person. Q1 and Q2 were considered to agree if both reported the presence or both reported the absence of symptoms involving a body system.

Second, it was determined whether individual features of case definitions (table 1) were present, and the reproducibility of each feature was assessed. To do

this, the presence or absence of each feature of the case definitions was ascertained separately for Q1 and Q2 for each person, and the questionnaires were considered to agree if the definitional feature was either present or absent on both occasions. Respondents were excluded from analyses if information on essential features was missing.

Finally, for each questionnaire separately, the features of the case definitions were combined to determine whether each person satisfied each of the seven case definitions. Agreement was achieved if the same case definition was satisfied on both occasions or on neither occasion.

RESULTS

Symptoms and their relation to exposure

The mean number of symptoms reported in Q1 was 42.8 (standard deviation (SD), 26.5) and in Q2 was 40.8 (SD, 27.4). When Q1 and Q2 were compared, the mean numbers of body systems for which symptoms were reported were 10.3 (SD, 2.8) and 9.8 (SD, 3.0), respectively. For most body systems (table 3), more symptoms were reported in Q1 than in Q2.

Total agreement across Q1 and Q2 for reporting involvement of any one body system ranged from 77 percent for lung to 92 percent for the nervous system; over 80 percent agreement was achieved for 10 of the 13 systems. Kappa statistics were statistically significant for all systems and were above 0.4 for 11 of 13 systems, indicating good levels of agreement beyond chance.

Agreement tended to be better for women ($n = 97$) than for men ($n = 37$). For women, the percentage of subjects for whom Q1 and Q2 agreed on the involvement of body systems ranged from 78 to 97 percent for the 13 body systems, with a median of 84 percent. For men, agreement ranged from 65 to 86 percent, with a median of 78 percent. Differences in agreement between men and women were at or close to a conventional level of significance for symptoms of the ear (84 percent agreement for women and 65 percent for men, $p = 0.02$), nose (93 percent for women and 81 percent for men, $p = 0.06$), mouth (83 percent for women and 73 percent for men, $p = 0.06$), and nervous system (97 percent for women and 79 percent for men, $p = 0.002$). For most body systems, there was no significant difference in the mean age of respondents for whom Q1 and Q2 agreed compared with those respondents whose questionnaires disagreed. However, the average age of men for whom the questionnaires agreed for mouth (age 45 years, $n = 27$) or muscle (age 46 years, $n = 30$) symptoms was lower ($p < 0.10$) than that of men for whom the questionnaires disagreed (age 54 years, $n = 10$ and age 55 years, $n = 7$, respectively). Similarly, the average age was somewhat lower ($p = 0.11$) for the 94 women for whom the questionnaires agreed regarding nervous system symptoms (age 41 years) than for the 3 women for whom the questionnaires disagreed (age 53 years).

Similar patterns of agreement were observed for symptoms reported to be linked to exposure. The mean numbers of exposure-linked symptoms for Q1 and Q2 were 21.3 (SD, 25.3) and 19.6 (SD, 24.2), respectively.

TABLE 3. Agreement* on symptoms reported by 134 responders to the reproducibility study of the University of Toronto Health Survey questionnaire, Ontario, Canada, 1995–1996

Body system	No. of symptoms		Agreement on body system involvement		
	Q_1† mean (SD†)	Q_2† mean (SD)	Total agreement (%)	Kappa	95% CI† for kappa
Eye	3.7 (2.7)	3.8 (2.7)	88.8	0.57	0.37, 0.76
Ear	1.9 (2.0)	1.7 (1.8)	79.1	0.53	0.38, 0.68
Nose	4.2 (2.7)	3.7 (2.6)	89.6	0.36	0.13, 0.62
Mouth	2.6 (2.5)	2.2 (2.4)	80.6	0.50	0.34, 0.66
Throat	2.9 (2.0)	2.6 (1.9)	84.8	0.44	0.23, 0.64
Lung	2.7 (2.6)	2.4 (2.6)	77.3	0.42	0.24, 0.59
Heart and circulation	2.1 (2.2)	1.9 (2.1)	78.9	0.54	0.39, 0.69
Blood and gland	2.5 (2.4)	2.2 (2.2)	82.7	0.58	0.43, 0.73
Muscle and joint	2.1 (2.1)	1.7 (2.0)	82.7	0.64	0.50, 0.77
Nervous system	11.3 (8.3)	10.1 (8.6)	91.8	0.43	0.16, 0.71
Stomach and bowel	4.4 (3.1)	4.2 (3.3)	83.3	0.30	0.08, 0.52
Bladder and genital	2.3 (2.2)	2.1 (2.0)	87.0	0.63	0.47, 0.79
Skin	3.0 (2.5)	2.4 (2.3)	83.6	0.48	0.30, 0.66

* Comparison of responses to the first and second questionnaires.
† Q_1, first questionnaire; SD, standard deviation; Q_2, second questionnaire; CI, confidence interval.

TABLE 4. Agreement* on reported symptoms linked to exposure of 134 responders to the reproducibility study of the University of Toronto Health Survey questionnaire, Ontario, Canada, 1995–1996

Body system	No. of symptoms		Agreement on body system involvement		
	Q_1† mean (SD†)	Q_2† mean (SD)	Total agreement (%)	Kappa	95% CI† for kappa
Eye	2.3 (2.5)	2.4 (2.6)	80.6	0.59	0.44, 0.73
Ear	0.9 (1.6)	0.8 (1.5)	82.8	0.62	0.48, 0.76
Nose	2.6 (2.6)	2.3 (2.5)	76.1	0.48	0.33, 0.64
Mouth	1.1 (2.1)	1.0 (1.8)	74.6	0.46	0.30, 0.61
Throat	1.5 (1.9)	1.4 (1.9)	81.8	0.64	0.50, 0.77
Lung	1.4 (2.5)	1.2 (2.3)	78.0	0.53	0.38, 0.68
Heart and circulation	0.8 (1.7)	0.8 (1.8)	78.9	0.49	0.33, 0.66
Blood and gland	1.0 (2.0)	1.0 (1.9)	77.4	0.48	0.33, 0.64
Muscle and joint	0.8 (1.6)	0.7 (1.5)	85.7	0.62	0.47, 0.78
Nervous system	4.4 (7.5)	4.6 (7.6)	76.1	0.51	0.37, 0.66
Stomach and bowel	2.5 (3.1)	1.9 (2.8)	76.5	0.53	0.39, 0.68
Bladder and genital	0.7 (1.4)	0.6 (1.4)	84.7	0.60	0.45, 0.76
Skin	1.5 (2.1)	1.3 (1.9)	76.1	0.52	0.38, 0.67

* Comparison of responses to the first and second questionnaires.
† Q_1, first questionnaire; SD, standard deviation; Q_2, second questionnaire; CI, confidence interval.

The mean numbers of body systems involved were 5.8 (SD, 4.0) and 5.4 (SD, 4.1), respectively. Again, for most body systems, symptoms were slightly more frequent in Q1 than Q2 (table 4). Agreement with respect to involvement of any single body system was more than 74 percent for all systems, and the kappa statistics exceeded 0.4.

When men (n = 37) and women (n = 97) were compared, agreement on the presence or absence of symptoms linked to exposure was similar. For men, the percentage for whom Q1 and Q2 agreed ranged from 59 to 86 percent over the 13 body systems, with a median of 81 percent. For women, agreement ranged from 73 to 86 percent, with a median of 79 percent. Significant differences in the percentage agreement comparing men with women were observed for only nasal symptoms (59 and 82 percent agreement for men and women, respectively; p = 0.005) and blood and circulation (86 and 73 percent agreement for men and women, respectively; p = 0.02). For most body systems, there was no significant difference in the mean age of men or women for whom Q1 and Q2 agreed compared with those for whom the questionnaires disagreed. However, the average ages were lower among men for whom Q1 and Q2 agreed on symptoms linked to exposure involving the blood and circulation (age 45 years, n = 32), nervous system (age 45 years, n = 25), and bladder (age 46 years, n = 32) compared with the average ages of men for whom the questionnaires disagreed on such symptoms: age 61 years (n = 5, p = 0.0001) for blood and circulation symptoms, age 53 years (n = 12, p = 0.05) for nervous system symptoms, and age 56 years (n = 5, p = 0.07) for bladder

symptoms. In contrast, women for whom Q1 and Q2 agreed regarding symptoms linked to exposure tended to be older on average than those for whom the questionnaires disagreed, significantly so for exposure-linked symptoms of the mouth (age 43 years, n = 71 vs. age 37 years, n = 26; p = 0.05) and stomach (age 43 years, n = 74 vs. age 37 years, n = 23; p = 0.05).

Features of case definitions

When features of each of the seven case definitions were examined separately, good agreement was achieved when Q1 was compared with Q2 (table 5).

TABLE 5. Agreement* on case definition features reported by 134 responders to the reproducibility study of the University of Toronto Health Survey questionnaire, Ontario, Canada, 1995–1996

Definitional feature	Total agreement (%)	Kappa	95% CI† for kappa
Symptoms linked to low-level exposure	86.6	0.39	0.17, 0.62
Multisystem	80.6	0.47	0.30, 0.64
Nervous system symptoms	76.1	0.51	0.37, 0.66
Chronic condition	85.5	0.68	0.54, 0.82
Acquired in response to an event	82.8	0.65	0.50, 0.80
Spreading of incitants	73.4	0.47	0.31, 0.63
Addictive responses	81.5	0.60	0.46, 0.75

* Comparison of responses to the first and second questionnaires.
† CI, confidence interval.

Total agreement for reporting of one or more exposure-linked symptoms in the last 12 months was 87 percent (kappa = 0.39). In terms of multisystem disease (when exposure-linked symptoms occurred in more than one body system), total agreement was 81 percent (kappa = 0.47). Overall agreement for the nervous system (76 percent) was somewhat lower although still good after adjustment for chance (kappa = 0.51). Agreement on chronicity was 85 percent (kappa = 0.68); agreement that the condition was acquired after an external event was 83 percent (kappa = 0.65). With respect to an escalation over time in the number of exposures provoking symptoms (spreading of incitants), agreement was 73 percent (kappa = 0.47). Agreement on the presence or absence of addictive responses was 82 percent (kappa = 0.60).

There were no significant differences between men and women in the percentage of those for whom Q1 and Q2 agreed on each feature of the case definitions, although agreement tended to be slightly better for women than for men (data available on request). For most features, no association existed between age and agreement between Q1 and Q2. However, men for whom Q1 and Q2 agreed on the presence or absence of nervous system symptoms were significantly (p = 0.05) younger (age 45 years, n = 25) than those for whom these symptoms were reported only once (age 53 years, n =12). In addition, men for whom Q1 and Q2 agreed on the presence of addictive behaviors were younger on average (age 46 years, n = 29) than men who reported this feature only once (age 55 years, n = 7). Women for whom Q1 and Q2 agreed regarding escalating numbers of exposures that triggered symptoms were significantly (p = 0.02) older on average (age 42 years, n = 61) than those who did not (age 35 years, n = 20). Women whose questionnaires agreed on the presence or absence of addictive behaviors were significantly (p = 0.05) younger (age 40 years, n =

77) than those whose questionnaires disagreed (age 47 years, n = 17).

Case definitions

Respondents were classified as satisfying each case definition for environmental sensitivity if they showed the features (table 1) "required" or "discussed" by each author. Total Q1 and Q2 agreement for respondent classification varied among case definitions from 80 to 90 percent (table 6, column 4). The high agreement (87 percent) observed for definitions proposed by the National Research Council (5) and by Ashford and Miller (7) occurred because a single symptom, if linked to an exposure, was sufficient to qualify as a case. Almost all participants (88 percent) satisfied this nonspecific criterion in Q1 (table 6, column 1). After adjustment for chance agreement, reproducibility was much lower for the National Research Council and Ashford and Miller definitions (kappa = 0.39, table 6) compared with the remaining five definitions.

For the five case definitions requiring more than one criterion for classification as environmental sensitivity, overall agreement comparing Q1 and Q2 was 80–90 percent (table 6, column 4), and 30–64 percent of respondents met the criteria for the case definitions at Q1. The proportions of respondents who at Q1 fulfilled any of the five case definitions and who subsequently fulfilled the same case definitions at Q2 (table 6, column 2) were highest for the 1999 consensus criteria (10) (91 percent), the Thomson et al. definition (4) (85 percent), and the Nethercott et al. definition (9) (89 percent) compared with the definitions of Cullen (6) (63 percent) and Randolph (8) (71 percent). Similarly, agreement was good for respondents classified as not satisfying case definitions at both Q1 and Q2, ranging between 79 and 91 percent for all definitions except those of Ashford and Miller (7) and the National

TABLE 6. Agreement* on criteria for environmental sensitivity case definitions for 134 responders to the reproducibility study of the University of Toronto Health Survey questionnaire, Ontario, Canada, 1995–1996

Case definition (reference no.)	% Positive in Q1†	% Positive in Q2† relative to positive in Q1	% Negative in Q2 relative to negative in Q1	Total agreement (%)	Kappa	95% CI† for kappa
Thomson et al. (4)	49.6	84.5	84.8	84.6	0.69	0.56, 0.82
National Research Council (5)/Ashford and Miller (7)	88.1	91.5	50.0	86.6	0.39	0.17, 0.62
Cullen (6)	41.4	63.4	91.4	79.8	0.57	0.40, 0.73
Randolph (8)	30.4	70.6	83.3	79.5	0.53	0.36, 0.70
Nethercott et al. (9)	64.1	89.3	78.6	85.5	0.68	0.54, 0.82
1999 Consensus (10)	63.2	90.5	88.4	89.7	0.78	0.66, 0.90

* Comparison of responses to the first and second questionnaires.
† Q1, first questionnaire; Q2, second questionnaire; CI, confidence interval.

Research Council (5). After adjustment for chance, the questionnaire was more reproducible overall for the 1999 consensus, Thomson et al., and Nethercott et al. definitions, with kappa statistics close to or exceeding 0.7, compared with the Cullen and Randolph definitions, with kappa statistics under 0.6.

Overall Q1 and Q2 agreement with respect to the Randolph (8) definition was higher, at 94 percent for men ($n = 32$) compared with 74 percent for women ($n = 80$) ($p = 0.02$), but there were no significant gender differences for the other case definitions. The average age of respondents whose Q1 and Q2 questionnaires agreed with respect to the Thomson et al. (4) case definition was lower (age 47 years, $n = 28$ for men and age 40 years, $n = 71$ for women) than for subjects whose questionnaires did not agree (age 57 years, $n = 4$ for men and age 46 years, $n = 14$ for women).

DISCUSSION

Diagnosis of environmental sensitivity begins with the reporting of symptoms associated with a variety of low-level exposures. Before a case definition can be developed, it is essential to demonstrate that the instrument used to identify these symptoms can yield reproducible responses. In the present reproducibility study, the twice-administered UTHS questionnaire achieved good agreement on symptoms for each of 13 body systems and on the number of symptoms reported. Complete agreement on symptoms linked to low-level exposures was observed for 87 percent of participants. Examination of differences in patterns of agreement observed between men and women or with age was limited because of small numbers. The findings did not, however, reveal patterns of differences in agreement by gender or age that were consistent for the various case definitions.

We found only one study that addressed reproducibility in questionnaires relating to multiple chemical sensitivity (12). However, this questionnaire considered reliability in reporting exposures that caused symptoms and did not examine the kinds of symptoms evoked or incorporate the multidimensional case definition features that were explored in the UTHS reproducibility study. As in the present study, good test-retest agreement was observed among 56 respondents to a mailed questionnaire administered 4–12 weeks apart. A correlation of 0.99 ($p < 0.0001$) was observed for a score reflecting the number of substances associated with symptoms identified from among 122 common substances.

Other studies of the reproducibility of self-report or self-administered questionnaires targeted at symptoms and risk factors experienced in the community have yielded levels of agreement similar to those for the UTHS questionnaire. Examples include reporting of low back pain (13), respiratory symptoms associated with asthma (14), symptoms experienced "now" or "in the past" (15), activities of daily living for elderly disabled men (16), melanoma risk factors (17), and types of physical activities (18).

The UTHS was able to not only document reliably a wide range of symptoms associated with exposures but also identify patients who experienced the features described in the seven published case definitions of environmental sensitivity. The UTHS achieved test-retest agreement close to or exceeding 80 percent. After adjustment for chance (13), kappa statistics of 0.5 to 0.8 indicated good agreement for each case definition except those of the National Research Council (5) and Ashford and Miller (7), for which the kappa statistic was 0.39. The latter two case definitions showed the highest level of overall agreement because they require patients to report only one exposure-associated symptom. With almost all participants satisfying this nonspecific criterion, a considerable portion of agreement was attributable to chance. In contrast, the criteria from the 1999 consensus (10) and the Thomson et al. (4) and Nethercott et al. (9) definitions resulted in the highest levels of chance-adjusted agreement.

However, in evaluating whether a questionnaire is appropriate for a specific objective, the choice of case definition may depend, at least in part, on whether the sensitivity (identification of cases) or the specificity (identification of persons who are not cases) should have priority. The 1999 consensus (10) and the Thomson et al. (4) and Nethercott et al. (9) definitions met both objectives, with high levels of reproducibility in identifying people who were classified as cases in Q1 (90, 85, and 89 percent, respectively) and in identifying people who were not initially classified as cases (88, 85, and 79 percent, respectively). These three case definitions therefore had greater reproducibility than the others when symptom history was assessed by the UTHS.

Although the UTHS demonstrated good reproducibility in identifying respondents who satisfied the criteria of seven published case definitions, it could not assess features of the case definitions that require challenge with exposures under controlled conditions, physical examination, application of diagnostic tests, or provocation by unrelated substances. Future research is needed to develop methods for assessing these latter aspects of the case definitions and to evaluate their reproducibility and validity.

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