



The Environmental Exposure and Sensitivity Inventory (EESI): a standardized approach for measuring chemical intolerances for research and clinical applications[†]

CLAUDIA S. MILLER^a AND THOMAS J. PRIHODA^b

^a *Environmental and Occupational Medicine, Department of Family Practice, University of Texas Health Science Center at San Antonio, San Antonio, Texas*

^b *Departments of Pathology and Psychiatry, University of Texas Health Science Center at San Antonio, San Antonio, Texas*

The lack of a generally accepted case definition for multiple chemical sensitivity (MCS) and the absence of a standardized approach for measuring salient aspects of chemical sensitivity that would permit cross-comparison of findings by different investigators have hindered progress in this area. Based upon findings from an earlier study of 112 persons with self-reported chemical sensitivity who attributed their chemical sensitivity to a well-defined exposure event, we developed an instrument with self-rating scales to assess Symptom Severity, Chemical (Inhalant) Intolerances, Other Intolerances (e.g., foods, medications, alcohol), Life Impact, and Masking (a measure of ongoing chemical exposures). When administered to four patient groups and controls, the scales showed good reliability and validity overall ($n=421$) and in each group. Used together, the scales provided sensitivity of 92% and specificity of 95% in differentiating chemically sensitive persons from controls. Our results support use of these scales individually or collectively for a variety of applications including the selection of chemically sensitive subjects and controls for research, assessment of chemical sensitivity in various study populations, cross-comparison of groups studied by different investigators, pre- and post-assessment of therapeutic interventions, clinical evaluation of complex patients who report intolerances, and teaching medical residents and students how to evaluate patients for chemical sensitivity and MCS.

Keywords: *chemical sensitivity, environmental exposures, environmental illness, Gulf War veterans, implant, multiple chemical sensitivity, pesticide, questionnaire, reliability, validity.*

Introduction

Investigators have adopted a variety of approaches to screen populations for chemical sensitivity and to select subjects and controls for studies of chemical sensitivity and multiple chemical sensitivity (MCS) (Simon et al., 1990; Fiedler et al., 1994; Kipen et al., 1995; Bell et al., 1996; Kreutzer and Neutra, 1996; Meggs et al., 1996). There is no generally accepted case definition for MCS, and the majority of instruments available for screening are very brief (e.g., one to five questions) or probe only one or two dimensions of the problem (Kipen et al., 1995; Bell et al., 1996; Kreutzer

and Neutra, 1996). Lack of a uniform approach for identifying chemically sensitive persons has hindered progress in this area by not permitting cross-comparison of findings in different study populations. A tool that could gauge the multi-system symptoms and multiple intolerances reported by these patients with good validity and reliability would be useful for research. One alternative that has been proposed is the development of a scale or instrument that would assess dimensions of MCS generally considered relevant, e.g., the number of organ systems with symptoms, the average severity of symptoms, and the propensity to avoid exposure (Kreutzer and Neutra, 1996).

In response to the need for a multi-dimensional instrument, we developed survey questions forming four scales useful for classifying Symptom Severity, Chemical Intolerances, Other Intolerances, and Life Impact based upon our results from a prior study of 112 individuals with self-reported MCS who attributed onset of their illness to a well-defined chemical exposure event (Miller and Mitzel, 1995). In addition, we designed a fifth scale (Masking Index) to assess the extent of ongoing exposures individuals might have.

Taken together, these five scales form the core of a new, self-administered questionnaire, the Environmental Expo-

1. Abbreviations: EESI, Environmental Exposure and Sensitivity Inventory ; MCS, Multiple Chemical Sensitivity ; QEESI, Quick Environmental Exposure and Sensitivity Inventory ; ROC, Receiver-operator characteristic.

2. Address all correspondence to: Claudia S. Miller, M.D., M.S., Environmental and Occupational Medicine, Department of Family Practice, Suite 610-L, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78284-7794. Tel.: (210)567-7760. Fax: (210)567-7764. E-mail: millercs@uthscsa.edu

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sure and Sensitivity Inventory (EESI) and a shorter version, the Quick Environmental Exposure and Sensitivity Inventory (QEESI), the latter containing only these five scales (a total of 50 items). The purpose of this paper is to describe the reliability, validity, sensitivity, and specificity of these scales for evaluating subjects for the presence or absence of features consistent with MCS. A companion paper, also published in this volume, compares findings from several patient groups and a control group (study population described below) using these scales (Miller and Prihoda, 1999).

Methods

Study Population

Subjects were 421 men and women who completed and returned the EESI. Patients were recruited via advertisements in patient group newsletters and by word-of-mouth. Announcements stated that the purpose of the study was to compare health problems and intolerances reported by patients with MCS, persons with implanted devices of any type, and Gulf War veterans. It was clearly indicated that participants did not need to be sick in order to enroll in the study. Respondents were sent one copy of the questionnaire and asked to return it in a pre-paid envelope. Controls were attendees at two professional conferences, one for women leaders in Texas and the other for persons who investigate pesticide incidents in the Midwestern United States.

Instrument

Four parallel versions of the EESI were employed. Each contained identical questions and scales, except as noted below. The 'General' version, administered to MCS patients who did not identify a specific initiating event for their illness and to controls, asked respondents to rate their *current* symptoms, chemical intolerances, other intolerances, and the impact of their sensitivities on activities of daily living. A parallel but somewhat longer version of the same questionnaire was sent to those MCS patients who attributed onset of their illness to a particular event, such as a chemical spill or pesticide exposure. This 'Exposure Event' questionnaire, as well as two other versions ('Implant' and 'Gulf War Veteran') of the EESI, had items and a format identical to those of the General version, but additionally asked respondents to rate the severity of their symptoms, intolerances, and life impact of their sensitivities both *before* and *since* the exposure event, implants, or Gulf War, respectively. These parallel forms of the EESI also contained additional specific questions concerning the nature of the exposures respondents felt had made them ill, e.g., type of implant and whether the implant had been removed, and exposures and symptoms soldiers may have experienced while in the Persian Gulf.

Scales

The EESI's Symptom Severity, Chemical Intolerance, Other Intolerance and Life Impact scales each contain ten items. Next to each item is a 0 to 10 rating scale. Participants are instructed to circle the number (0–10) that best corresponds with the severity of their symptoms, responses to various substances, and the impact of their sensitivities on their activities: 0=not at all a problem, 5=moderate, 10=severe or disabling. Scores on the ten items for each scale are tallied to obtain a total scale score (0–100).

Symptom Severity Scale Items on this scale were derived from our earlier study of persons with self-reported MCS attributed to a well-defined exposure either to an organophosphate or carbamate pesticide ($n=37$) or to indoor air contaminants associated with new construction ($n=75$) (Miller and Mitzel, 1995). Responses to 114 symptom items on the questionnaire used in that study were subjected to factor analysis resulting in eight symptom scales, each with high internal consistency (Cronbach's alpha reliability coefficient=0.83 to 0.92). The eight included: Head-related, Cognitive, Affective, Neuromuscular, Musculoskeletal, Gastrointestinal, Heart-related, and Airway/Mucous Membrane symptom scales. *Post-hoc* analyses resulted in the addition of two more symptom scales, Skin and Genitourinary. The Cronbach's alpha for the items included on the Skin scale was 0.69 and the Genitourinary scale, 0.65. Ten questions, one representing each of the symptom scales, then were constructed to embody the most frequently endorsed symptoms on each scale. Because fatigue loaded on several scales, e.g., Affective (depression), Cognitive (memory and concentration difficulties), and Musculoskeletal (muscle weakness), a separate question on fatigue was added to the EESI for completeness.

Chemical (Inhalant) Intolerance Scale The aforementioned study also included a checklist of 98 common environmental chemical exposures. Ten of these exposures were selected to form a Chemical (Inhalant) Intolerance scale based on several criteria including chemical structural diversity, ubiquity of exposure, and the frequency with which persons with MCS attributed symptoms to them: insecticide (pesticides); paint or paint thinner (solvents); gasoline vapors (long-chain hydrocarbons); fresh tar or asphalt (polycyclic hydrocarbons); tobacco smoke (combustion products); diesel or gas engine exhaust (petrochemical combustion products); cleaning products such as disinfectants or bleach (chemically diverse cleaning agents); perfumes, air fresheners, or other fragrances (fragrances); nail polish, nail polish remover, or hair spray (cosmetic fragrances/solvents); and new furnishings such as new carpeting, a new soft plastic shower curtain, or the interior of a new car (solvents, plasticizers, formaldehyde). In our

**Table 1.** Scale^a reliability coefficients (Cronbach's alpha).

Group (n)	Scale			
	Symptom Severity	Chemical Intolerance	Other Intolerance	Impact on Life
Controls (76)	0.85	0.95	0.85	0.91
MCS-no event (90)	0.86	0.84	0.76	0.84
MCS-event (96)	0.88	0.90	0.86	0.92
Implant (87)	0.86	0.96	0.86	0.95
Gulf War veterans (72)	0.91	0.96	0.90	0.95
Total (421)	0.94	0.97	0.89	0.97

^a Each scale score (0–100 possible points) is the raw total of ten items, individually scored from 0 to 10.

earlier study, at least 80% of persons in both the pesticide and remodeling exposure groups reported that these exposures triggered symptoms.

Other Intolerance Scale This scale embodies ten questions concerning exposures other than chemical inhalants that MCS patients frequently say make them ill. Included are items related to various ingestants (chlorinated tap water, foods or food additives, food cravings or feeling ill if a meal is missed, feeling ill after a meal, caffeine intolerance, caffeine withdrawal symptoms, feeling ill after a small amount of an alcoholic beverage); various skin contactants; medical drugs or devices; and allergens for which classical allergic responses (asthma, nasal symptoms, hives, anaphylaxis, or eczema) have been noted.

Life Impact Scale Items on this scale were selected, based upon findings from our earlier study, to represent ten life domains commonly reported by MCS patients as disrupted by their chemical and food intolerances: diet, ability to work or attend school, choice of home furnishings, choice of clothing, ability to travel or drive, choice of personal care products (e.g., make-up, deodorant), social activities, choice

Table 2. Scale validity Pearson correlation for total $n=421$.

Item	Scale			
	Symptom Severity	Chemical Intolerances	Other Intolerances	Impact on Life
Life quality (0–10)	-0.82***	-0.57***	-0.62***	-0.68***
Health status (0–10)	-0.81***	-0.59***	-0.61***	-0.66***
Energy level (0–10)	-0.78***	-0.50***	-0.55***	-0.59***
Body Pain (0–10)	0.63***	0.31***	0.40***	0.36***
Ability to work	-0.59***	-0.58***	-0.53***	-0.67***
Employment	-0.51***	-0.52***	-0.45***	-0.57***

*** $p \leq 0.001$.

of hobbies or recreation, relationship with spouse or family, and ability to perform household chores.

Masking Index A fifth scale, a Masking Index, was designed to help assess the extent to which respondents may have ongoing exposures. One theory about chemical sensitivity is

Table 3. Scale validity Pearson correlation.(a) Control group ($n=76$)

Item	Scale			
	Symptom Severity	Chemical Intolerances	Other Intolerances	Impact on Life
Life quality	-0.33**	-0.11 NS	-0.29*	-0.26*
Health status	-0.48****	-0.24*	-0.35**	-0.34**
Energy level	-0.26*	-0.07 NS	-0.15 NS	-0.19 NS
Body pain	0.28*	0.18 NS	0.21 NS	0.17 NS
Employment	0.003 NS	-0.13 NS	-0.10 NS	-0.01 NS

(b) MCS-no initiating event group

Life quality	-0.55****	-0.26*	-0.47****	-0.53****
Health status	-0.60****	-0.31**	-0.50****	-0.42****
Energy level	-0.49****	-0.28**	-0.46****	-0.46****
Body pain	0.38***	0.26*	0.26*	0.28**
Ability to work	-0.22*	-0.31**	-0.34***	-0.21*
Employment	-0.28**	-0.25*	-0.24*	-0.22*

(c) MCS initiating event group

Life quality	-0.67****	-0.57****	-0.51****	-0.56****
Health status	-0.60****	-0.45****	-0.48****	-0.48****
Energy level	-0.62****	-0.34***	-0.45****	-0.39****
Body pain	0.62****	0.26*	0.30**	0.25*
Ability to work	-0.33***	-0.51****	-0.44****	-0.52****
Employment	-0.21*	-0.31**	-0.21*	-0.38****

(d) Implant group

Life quality	-0.64****	-0.33**	-0.43****	-0.45****
Health status	-0.51****	-0.43****	-0.39***	-0.49****
Energy level	-0.41****	-0.09 NS	-0.17 NS	-0.22*
Body pain	0.38**	0.24*	0.35**	0.32**
Ability to work	-0.31**	-0.04 NS	-0.16 NS	-0.24*
Employment	-0.47****	-0.29**	-0.31**	-0.40***

(e) Gulf War veteran group

Life quality	-0.75****	-0.55****	-0.50****	-0.74****
Health status	-0.69****	-0.58****	-0.45****	-0.63****
Energy level	-0.71****	-0.51****	-0.41***	-0.62****
Body pain	0.50****	0.33**	0.31**	0.37**
Ability to work	-0.54****	-0.45****	-0.29***	-0.65****
Employment	-0.50****	-0.43***	-0.30*	-0.51****

* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$, NS is not significant or $p > 0.05$.



that overlapping symptoms resulting from everyday exposures to chemicals at low levels may mask individuals' awareness of their acute responses to particular exposures (Miller, 1997). The ten items on the Masking Index (scored yes=1 or no=0) ask subjects whether they regularly (once a week or more often) use tobacco products, alcoholic beverages, caffeine, certain drugs, or scented personal care products (fragrances, hair spray); whether they are exposed to chemicals at work; whether they live with a smoker; whether propane or gas fuel is used for cooking; whether pesticides have been applied in their home or workplace in the past year; and whether scented fabric softeners are used in laundering their clothes or bedding.

The above five scales comprise the QEESI. The EESI contains identical scales, but in addition includes items pertaining to life quality, overall health status, energy level, body pain, ability to work, employment status, confusion while driving, smokers' responses to tobacco, sensitivity to bright light and noise, past history of chemical intolerance, and past medical history.

Scale Validity and Reliability

In this paper, we show Cronbach's alpha reliability for each scale over all subjects and for each patient group. As a first step in testing the validity of these scales, scores on each scale were compared with responses to single survey question items on each of the following: life quality, health status, energy level, body pain, ability to work, and employment status. Such items are commonly used during routine patient history-taking. The first four of these were scaled from 0–10, while the last two measures were dichotomous.

Table 5. Logistic regression results for discrimination of controls from all other subjects.

Scale	Sensitivity (%)	Specificity (%)	Cutpoint
Symptom Severity	89.5	88.2	40
Chemical Intolerance	82.0	84.2	40
Other Intolerance	80.8	75.0	25
			Predicted probability
Multiple scales and products used together	91.6	94.7	0.84

We further tested the validity of the Chemical Intolerance and Other Intolerance scales by determining whether they would discriminate between control subjects and all other study subjects through the use of logistic regression (Hosmer and Lemeshow, 1989), odds ratio, and area under the receiver–operator characteristic (ROC) curve. In order to assess discriminatory power of these scales, we used the control subjects as non-chemically sensitive persons and treated the other groups as though they might be chemically sensitive. Specificity and sensitivity results obtained are with respect to the control subjects versus the other subjects using logistic regression including the main effects and two-way interactions and stepwise selection of significant effects. Only significant effects were retained in the prediction.

Next, we applied the symptom, chemical intolerance, and other intolerance criteria, derived from our analysis of the validity and reliability of the EESI, retroactively to each group in order to determine the number of individuals within each group who met one, two or all three of these

Table 4. Significance of discrimination power of scales when used alone or when combined in a multiple logistic prediction equation.

Scale	p-value	Odds ratio for one-point increase	Odds ratio for five-point increase	Area under ROC Curve
<i>Individual scales</i>				
Chemical Intolerance	0.0001	1.054	1.301	0.884
Other Intolerance	0.0001	1.083	1.490	0.851
Symptom	0.0001	1.119	1.754	0.958
<i>Multiple scales^a</i>				
Chemical Intolerance	0.0001	1.122	1.778	0.982 (when the scales below are used jointly-see text)
Symptom Severity	0.0001	1.154	2.047	
(Other Intolerance × Chemical Intolerance) ^b	0.0006	0.999	0.995	
(Masking × Chemical Intolerance) ^b	0.0001	0.984	0.923	

^a Each of the four items listed below is a factor in one multiple logistic prediction equation (see text).

^b The product of these two scale ratings.

The odds ratios given in the table are odds ratios of being a non-control (chemically sensitive) subject for one-point and five-point increases in the scale for which the ratio is reported.



criteria. Cutpoints used were: symptoms ≥ 40 ('high' symptom score), chemical intolerance score ≥ 40 ('high' chemical intolerance score), and other intolerance score ≥ 25 ('high' other intolerance score).

Results

Questionnaires were completed and returned by 421 people: 96 self-identified MCS subjects who attributed onset of their illness to an antecedent event (MCS-event), 90 MCS subjects who did not identify an initiating exposure (MCS-no event), 87 implant recipients, 72 Gulf War veterans, and 76 controls. Recruitment procedures, demo-

Table 7. Criteria for low, medium, and high scores on five scales.

Scale	Score		
	Low	Medium	High
Symptom Severity	0-19	20-39	40-100
Chemical Intolerance	0-19	20-39	40-100
Other Intolerance	0-11	12-24	25-100
Life Impact	0-11	12-23	24-100
Masking	0-3	4-5	6-10

graphics of the study population, and means for each scale and group appear in a companion paper (Miller and Prihoda, 1999, this volume).

Table 6. (a) Distribution of subjects by group using 'high' cutoff points for Symptom Severity (≥ 40) and Chemical Intolerances (≥ 40), with Masking low or not low (< 4 or ≥ 4).

Risk criteria ^a	Symptom	Chemical	Masking	Percentage of each group meeting risk criteria				
				Controls	MCS-no event	MCS-event	Implant	Gulf War veterans
Degree to which MCS is suggested ^b	Symptom Severity score	Chemical Intolerance score	score					
Very suggestive	≥ 40	≥ 40	≥ 4	7	16	23	39	45
Very suggestive	≥ 40	≥ 40	< 4	0	65	66	36	4
Somewhat suggestive	≥ 40	< 40	≥ 4	3	1	2	16	26
Not suggestive	≥ 40	< 40	< 4	0	0	2	3	6
Problematic	< 40	≥ 40	≥ 4	7	3	1	1	0
Problematic	< 40	≥ 40	< 4	3	13	4	2	0
Not suggestive	< 40	< 40	≥ 4	68	1	0	2	18
Not Suggestive	< 40	< 40	< 4	12	1	2	1	1

^a Subjects must meet all three criteria, i.e., Symptom Severity, Chemical Intolerance and Masking score, as indicated in each row of this table.

^b 'Very suggestive' = high symptom and chemical intolerance scores. 'Somewhat suggestive' = high symptom score but possibly masked chemical intolerance. 'Not suggestive' = either (1) high symptom score but low chemical intolerance score with low masking or (2) low symptom and chemical intolerance scores. 'Problematic' = low symptom score but high chemical intolerance score. Persons in this category with low masking (< 4) may be sensitive individuals who have been avoiding chemical exposures for an extended period (months or years).

(b) Distribution of subjects by group using 'low' cutoff points for Symptom Severity (< 20) and Chemical Intolerances (< 20), with Masking low or not low (< 4 or ≥ 4).

Risk criteria ^a	Symptom	Chemical	Masking	Percentage of each group meeting risk criteria				
				Controls	MCS-no event	MCS-event	Implant	Gulf War veterans
Symptom score	score	Intolerance score	score ^b					
≥ 20	≥ 20	≥ 20	≥ 4	14	11	10	29	47
≥ 20	≥ 20	≥ 20	< 4	5	87	88	60	26
≥ 20	< 20	≥ 20	≥ 4	12	0	0	11	21
≥ 20	< 20	≥ 20	< 4	5	0	0	0	3
< 20	≥ 20	≥ 20	≥ 4	7	1	2	0	0
< 20	≥ 20	≥ 20	< 4	7	1	0	0	0
< 20	< 20	≥ 20	≥ 4	33	0	0	0	0
< 20	< 20	< 20	< 4	17	0	0	0	3

^a Subjects must meet all three criteria, i.e., Symptom, Chemical Intolerance and Masking score.

^b Persons with masking < 4 may be sensitive, but avoiding problem exposures.

The cutpoints of < 20 for Symptom Severity and < 20 for Chemical Intolerances identified healthy subjects with a high degree of specificity (individuals in last two rows). These cutpoints could be used for the selection of healthy control subjects for studies of chemical sensitivity.

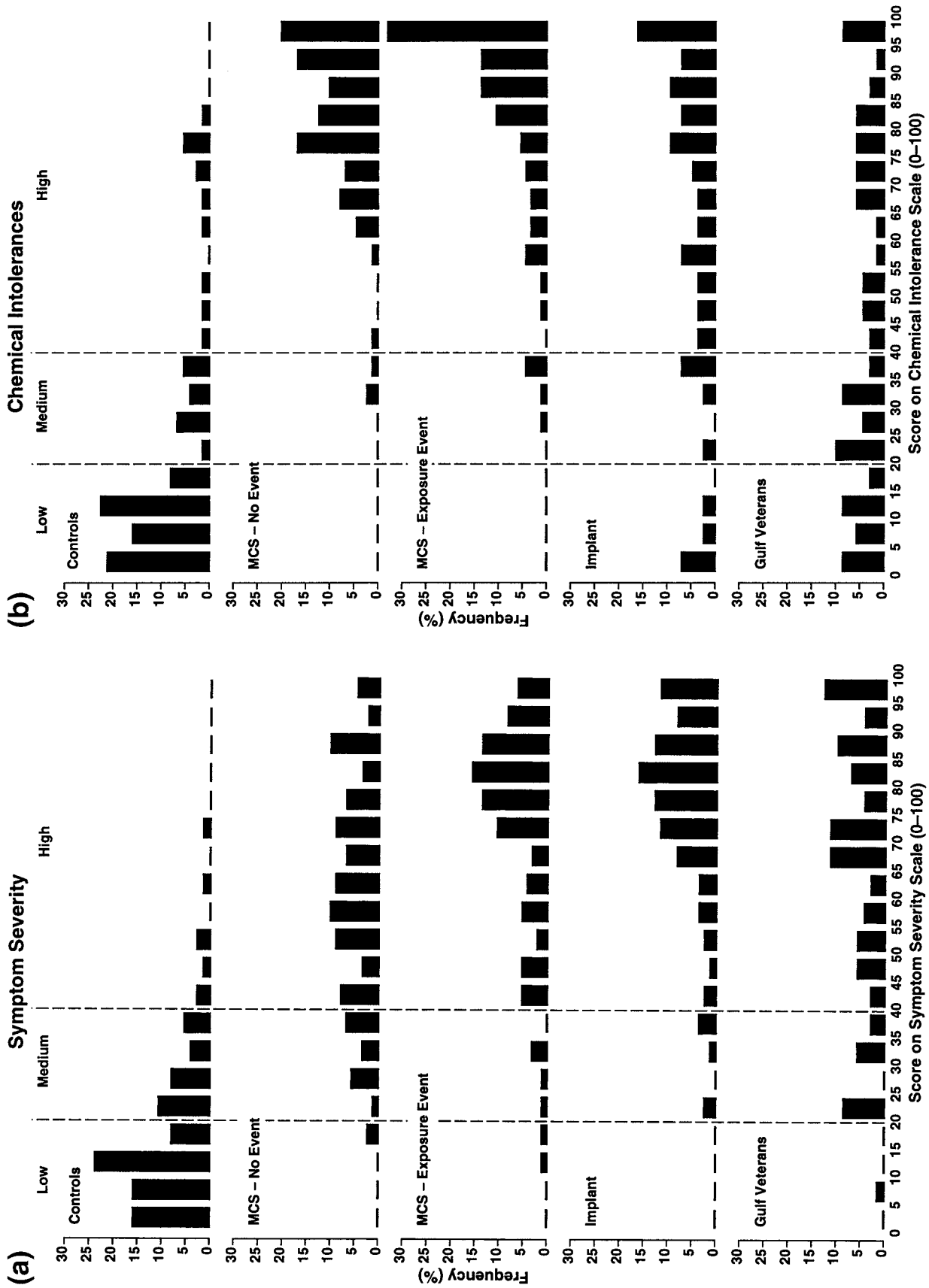


Figure 1. (a-e) Distribution of subjects' responses on scales with low, medium and high ranges shown.

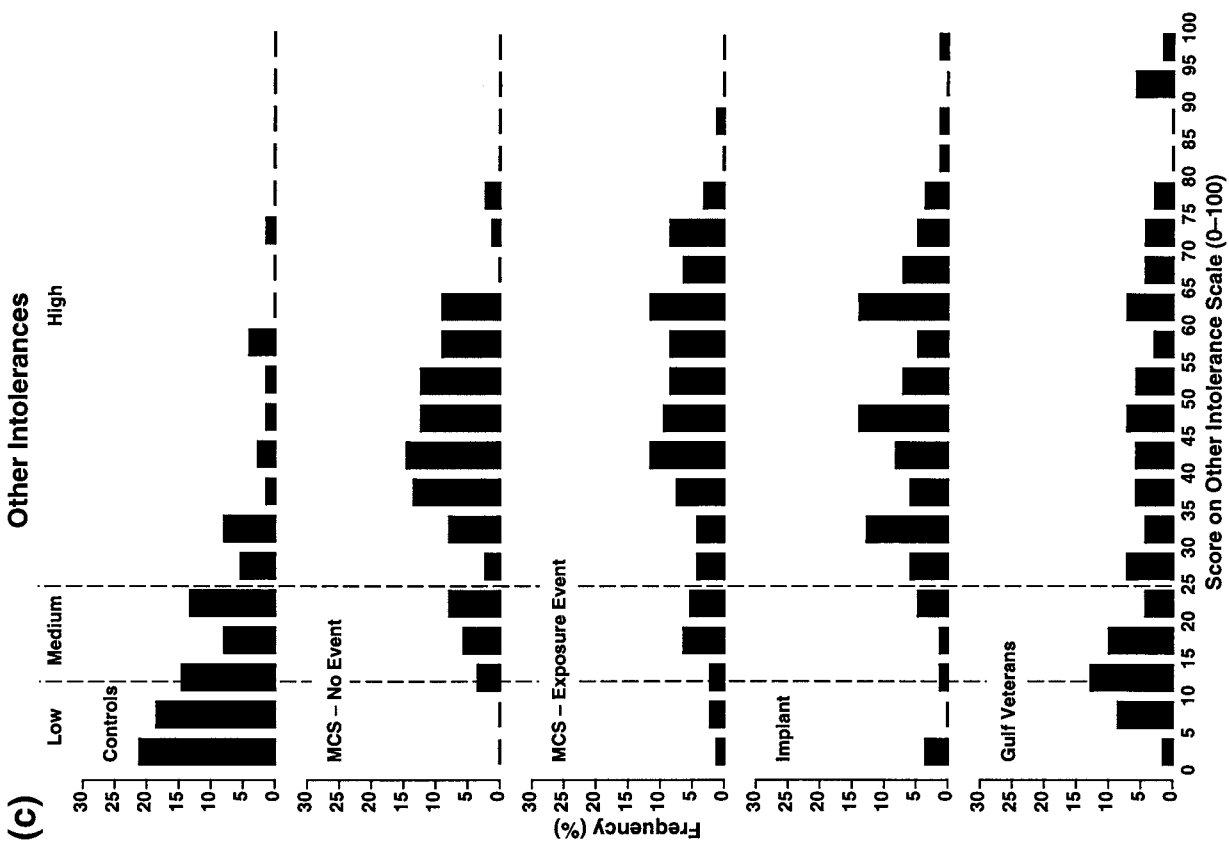
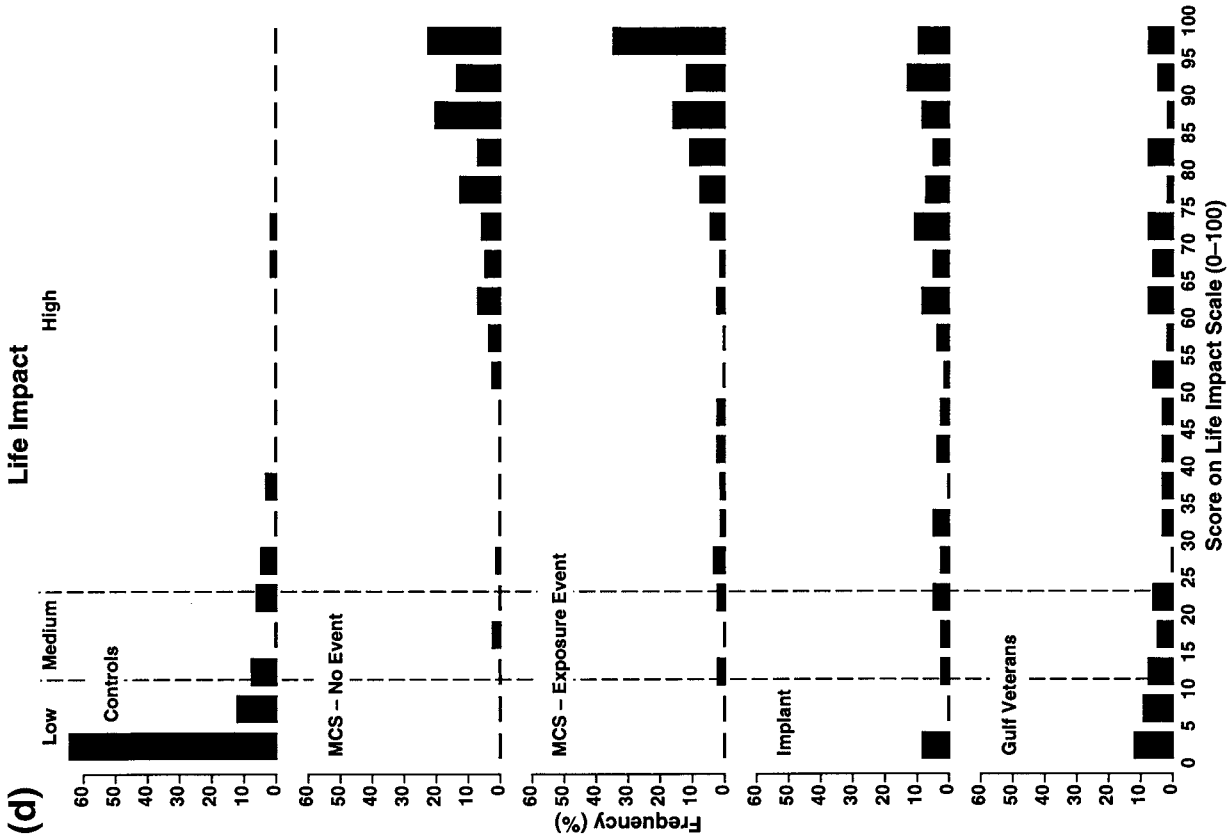


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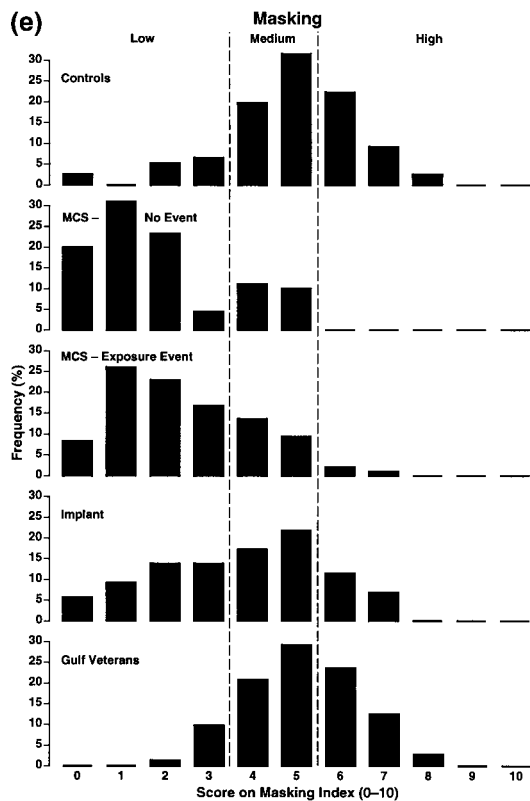


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Reliability

Table 1 provides the Cronbach’s alpha reliability coefficient for each of the four scales in each of the five groups, as well as over all subjects. Reliability ranged from 0.84 to 0.97 in all cases with the single exception of the Other Intolerance scale for the MCS-no event group (reliability of 0.76). Thus, overall reliability was high. This indicates that the questions selected form scales showing good internal consistency.

Validity

Table 2 displays the Pearson correlations for each of the four scales with the validity items of interest, i.e., life quality, health status, energy level, body pain, ability to work, and employment status. All correlations were significant and in the expected direction, thus supporting overall validity. This indicates that the scales have good construct validity for the problems reported by the patient groups.

Tables 3a through 3e provide the validity results for each of the five groups. For MCS subjects without an initiating event (Table 3b), those with an initiating event (Table 3c), and Gulf War veterans (Table 3e), all correlations were statistically significant and in the expected direction. In fact, 116 (97%) of the 120 correlations used to check validity in the patient groups were statistically significant, thus supporting validity of the scales. All four scales for all

patient groups correlated significantly with employment status, body pain, health status, and life quality. Only the Chemical Intolerance and Other Intolerance scales did not correlate significantly with two validity items (energy level and ability to work) in one group, implant recipients. Nevertheless, 20 of the 24 correlation coefficients for the implant group were statistically significant. As would be expected, there were fewer statistically significant correlations for the control group, which was generally healthier than the patient groups. Thus, the correlation analysis supports the construct validity of these scales.

In sum, each scale individually is a significant and valid discriminator variable for chemically sensitive subjects versus controls. In addition, the scales have main effects and somewhat complex interactions in discriminating between controls and chemically sensitive subjects. This more complex model can be used to increase the sensitivity and specificity for distinguishing controls from chemically sensitive subjects. The discriminating power of these scales is largest for the Symptom Severity scale (odds of a subject’s being chemically sensitive double for a five-point increase on this 0–100 scale) and for the Chemical Intolerance scale (odds double for a six-point increase). The product of Other Intolerance and Chemical Intolerance, and the product of Masking and Chemical Intolerance slightly modify the effect of Chemical Intolerance. The use of multiple scales in this manner can increase the ability to discriminate over use of a single scale (Table 4). Multiple logistic regression produced an optimal cutpoint at predicted probability of 0.84 based on using the Chemical Intolerance and Other Intolerance scores, their product, the Symptom score, and the product of the Masking and Chemical Intolerance scores. We optimized the cutpoint by selecting a point at which sensitivity and specificity both were high and nearly equal (Table 5). Sensitivity of 92% and specificity of 95% can be achieved by first computing:

$$R = -4.4667 + (0.1148 \times \text{Chemical Intolerance}) + (0.1436 \times \text{Symptom Severity}) - (0.0011 \times \text{Other Intolerance} \times \text{Chemical Intolerance}) - (0.157 \times \text{Masking} \times \text{Chemical Intolerance}),$$

and then computing the predicted probability:

$$\text{PrPr} = \text{Predicted probability} = e^R / (1 + e^R),$$

where $e=2.71828...$ is the base of the natural logarithm. If PrPr is 0.84 or higher, classify the subject as ‘chemically sensitive’. If PrPr is less than 0.84, classify the subject as ‘not chemically sensitive’. Results of a more simplified application of the scales are displayed in Table 6a which shows how subjects in each group distributed over

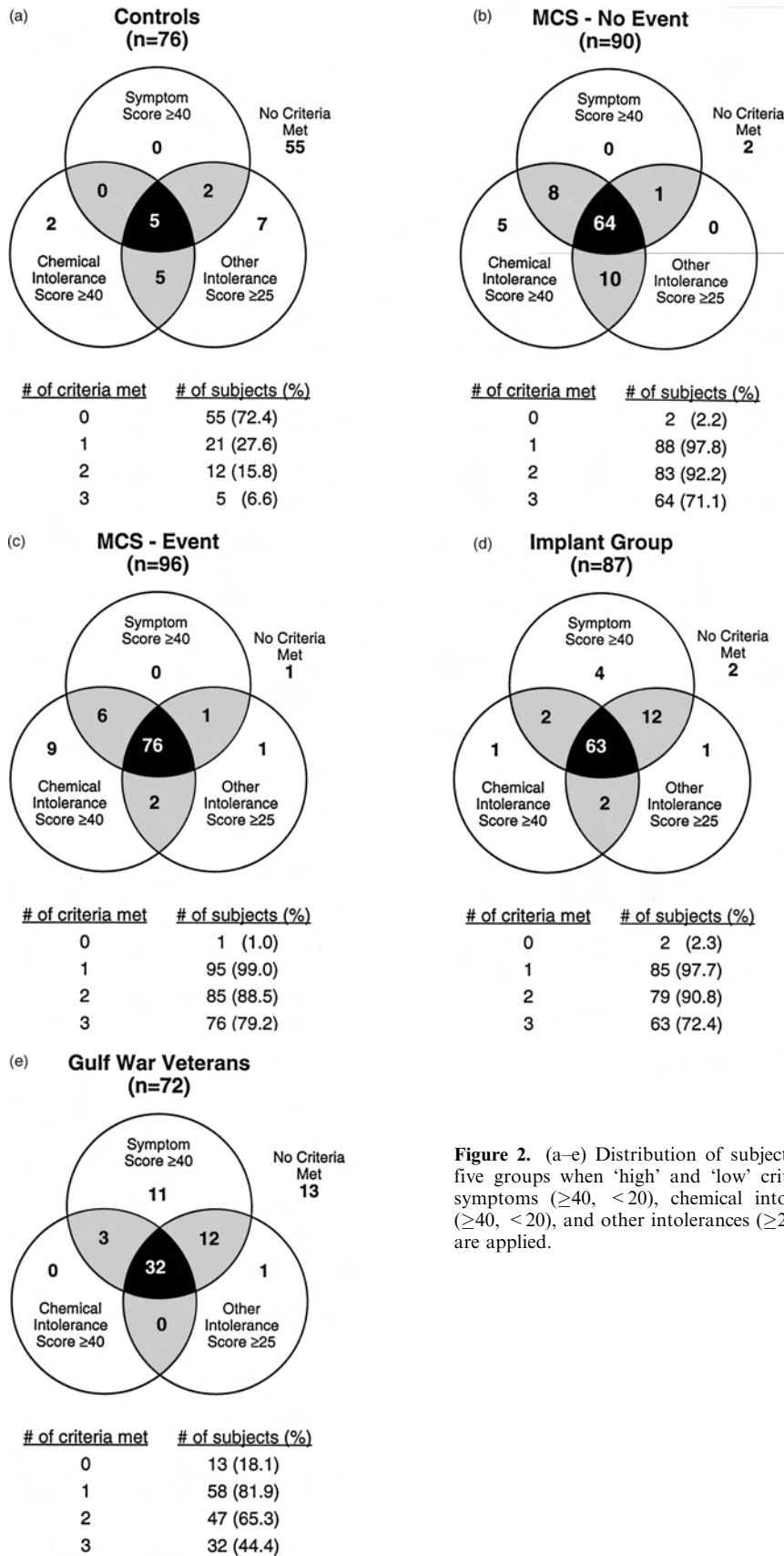


Figure 2. (a-e) Distribution of subjects in the five groups when 'high' and 'low' criteria for symptoms (≥ 40 , < 20), chemical intolerances (≥ 40 , < 20), and other intolerances (≥ 25 , < 12) are applied.



the various scales of risk for chemical sensitivity using high scores for symptoms (≥ 40) and chemical intolerance (≥ 40) as categories. Table 6b similarly shows percentages of subjects from each group reporting low levels of symptoms (< 20) and chemical intolerances (< 20). The latter cutpoints identified healthy subjects with a high degree of specificity. Based upon these analyses, Table 7 proposes criteria for high, medium, and low scores for each scale.

Figures 1a through 1e show the distribution of subjects in each group for each of the scales. Figures 2a through 2e show the distribution of subjects in each group when the high cutpoints for three scales (Symptom Severity ≥ 40 , Chemical Intolerance ≥ 40 , and Other Intolerance ≥ 25) were applied.

Discussion

These results support the use of the EESI's scales individually and collectively in studies to identify subjects likely to be chemically sensitive as well as to identify control subjects unlikely to be chemically sensitive. The Symptom, Chemical Intolerance, Other Intolerance and Life Impact scales were highly reliable in these subject groups and overall for all subjects. They also showed good validity in that (1) they correlated well with standard survey measures of health status and life function; and (2) they discriminated controls from chemically sensitive persons with good sensitivity and specificity. The Chemical Intolerance and Symptom Severity scales had the greatest discriminating power. It appears that the effects of chemical exposures can be masked, making chemical sensitivity a difficult diagnosis in persons with significant on-going exposures (see Miller and Prihoda, 1999).

The combined scores for Symptom Severity, Chemical Intolerance, Other Intolerance, and Masking used in a multiple logistic regression equation provided a sensitivity of 92% and specificity of 95% here. The coefficients in this equation were determined from our data by stepwise multiple logistic regression and may be different for other patient groups. Sensitivity and specificity are 83.2% and 84.2% based on a cutpoint of 40 for the Chemical Intolerance scale by itself. This ten-item scale compares favorably with a 122-item checklist of chemicals which afforded a sensitivity of 69% and specificity of 89% (Kipen et al., 1995). Because the calculation using the multiple logistic regression equation may be cumbersome, we provide Table 6a which displays a simplified classification of 'high' and 'low' for three scales (Symptom Severity, Chemical Intolerance, and Masking). This table more simply delineates diagnostic categories of risk for MCS, i.e., 'very suggestive', 'somewhat suggestive', and 'not suggestive' of MCS (category names after Kreutzer and Neutra, 1996).

Table 8. Sensitivity and specificity resulting from application of high and low cutoff points for Symptom Severity, Chemical Intolerance and Other Intolerance scales, and for all three scales taken together.

Criteria met	Sensitivity (%)	Specificity (%)
<i>Application of high cutoffs^a</i>		
Symptom Severity ≥ 40	87.2	91.0
Chemical Intolerance ≥ 40	83.2	84.2
Other Intolerance ≥ 25	83.5	75.0
All three criteria	67.2	90.9
<i>Application of low cutoffs^b</i>		
Symptom Severity < 20	63.2	98.3
Chemical Intolerance < 20	67.1	91.9
Other Intolerance < 12	46.1	93.6
All three criteria	31.6	99.7

^aThese criteria could be used to select chemically sensitive individuals as research subjects with a high degree of specificity.

^bThese criteria could be used to select healthy subjects as research controls with a high degree of specificity. For certain studies, it may be desirable to exclude individuals whose scores fall in a 'gray zone' between the high and the low cutoff points.

Table 8 provides sensitivities and specificities for the Symptom Severity, Chemical Intolerance, and Other Intolerance scales, used individually or collectively, when high and low cutoffs are applied. We suggest that application of all of these criteria (high cutoffs for selection of chemically sensitive subjects, low cutoffs for selection of controls) will provide the greatest specificity (90.9% for subjects, 99.7% of controls) for future investigations involving MCS.

While the Symptom Severity scale by itself (cf. Table 8) appeared to offer the greatest sensitivity and specificity, the patient groups we studied were generally much sicker than controls. If comparisons had been made with other sick groups, it is unlikely that Symptom Severity alone would have been able to distinguish as well between chemically sensitive subjects and other sick patients. Hence, we recommend that all three criteria in Table 8 be used in selecting research subjects. While these stringent criteria will reduce the number of individuals qualifying as subjects and controls, a high degree of specificity will be attained. In addition, use of the QEESI as a screening tool to identify study participants should greatly streamline the recruitment process.

Applying the 'high' criteria (Symptom Severity score ≥ 40 , Chemical Intolerance score ≥ 40 , and Other Intolerance score ≥ 25) retroactively, we determined that only 6.6% of our controls met all three criteria, and 15.8% met two of three criteria (Figure 2a). These percentages compare favorably with results of a random digit telephone survey of 4046 households in California in which 6.3% of residents



said they had been told by a doctor that they had environmental illness or MCS, and 15.8% considered themselves 'allergic' or 'unusually sensitive to everyday chemicals' (Kruetzer et al., 1999). Because not everyone at the meetings from which we recruited our controls completed a questionnaire, there could have been some responder bias in our control group. However, our findings for a general population sample are consistent with results from the California study and other prevalence studies (Environmental Protection Agency, 1989; Bell et al., 1996; Meggs et al., 1996).

Researchers interested in chemical sensitivity have employed a variety of instruments, most lacking any assessment of validity, reliability, sensitivity, or specificity. Several large surveys have employed a single screening question, e.g., 'Do you consider yourself especially [or unusually] sensitive to certain chemicals?' (Environmental Protection Agency, 1989; Kruetzer, et al., 1999). Using a checklist of 122 common substances to screen for chemical sensitivity, Kipen et al. found that both MCS and asthma patients endorsed significantly more items as causing symptoms than did other patient groups. The authors proposed that a score of 23 out of the 122 items would afford adequate sensitivity (69%) and specificity (89%) for differentiating MCS patients from non-MCS patients. Scores for 69% of their MCS patients met or exceeded this level. However, the scores of 54% of their asthma patients and 15–20% of their other clinic patients also met or exceeded this criterion. We did not have a group of patients with asthma in our study, but we would expect that some might also be chemically sensitive or hard to discriminate from MCS subjects since bronchoconstriction can occur in response to common irritants including fragrances, insecticides, cleaning agents, and vehicle exhaust. Similarly, patients with rhinitis or migraine headaches often report that certain odors make them feel worse. The challenge to researchers is how to differentiate these individuals from those with MCS. To do so, researchers need to know both how disabling the exposures are and whether multi-system symptoms occur, as described for MCS. Single screening questions or checklists of chemicals do not provide this depth of information.

Chemically intolerant patients often are not only troubled by their symptoms, but also by limitations imposed by their condition on their activities, including their ability to work, attend school, socialize, travel, live in conventional homes, wear usual clothing, and eat a normal diet. Simon et al. (1990) attempted to gauge the life impact of chemical sensitivity, as a means of selecting research subjects, by using four screening questions. Subjects answered 'yes' or 'no' as to whether they needed to follow a specific diet, took special precautions in their homes or home furnishings, wore particular clothes, or had trouble shopping in stores or eating in restaurants because of their sensitivities. Based

upon the distribution of responses obtained, the authors deemed a positive response to three or more of the four items as indicative of self-reported environmental illness. The Simon items do not gauge the severity of these intolerances; they overlook critical aspects of daily living which patients consider most disrupted by their sensitivities, e.g., ability to work or go to school and choice of recreation (see Miller and Prihoda, 1999); and they do not measure the number, nature, or severity of symptoms.

A set of screening items used by Bell et al. (1996) asks subjects to rate frequency of illness in response to the odors of various substances, including pesticides, paint, perfume, car exhaust and new carpet, on a five-point Likert scale (i.e., 1=almost never and 5=almost always). Used alone, this set of items does not address the number, nature, or severity of symptoms, life impact, or other intolerances frequently cited by chemically sensitive individuals.

Some investigators (Cullen et al., 1992; Fiedler et al., 1992; Fiedler et al., 1994) have elected to enroll patients in their studies based upon one of the early case definitions proposed for MCS (Cullen, 1987). This definition excludes 'definable' clinical conditions, such as asthma, which appear to overlap with MCS. However, asthma may also be exposure-induced and is commonly reported by patients with MCS. At present, there is no widely accepted case definition for MCS (the various case definitions that have been proposed for MCS are summarized in Ashford and Miller, 1998). Indeed, it might not be possible to craft one, if, as has been suggested, chemical sensitivity is simply a hallmark symptom for a broad category of chemically induced conditions (which can affect any organ system), much as fever is a hallmark symptom for infectious diseases (Miller, 1997). Just as it would not be feasible to develop a single case definition that would embrace all infectious diseases, constructing a case definition for all of the illnesses in this category may not be possible.

In the absence of an accepted case definition for MCS, there remains a need for an approach that can reliably gauge chemical intolerance in individuals. In selecting an instrument, investigators and clinicians must consider the validity, reliability, sensitivity, and specificity of available measurement tools. Our findings demonstrate that the scales described here can serve as reliable and valid tools for assessing chemical sensitivity, at least in comparison with normal control subjects.

The reliability of the EESI is reflected by the very high Cronbach's alpha within each patient group and over all of the subjects in this study. Although the reliability of an instrument is defined, and must be re-calculated, for each group of subjects for which it is used, our data provide evidence in five groups of subjects which indicates that this instrument can be expected to be very reliable in many studies of chemical sensitivity and other conditions.



As self-rating questionnaires, the EESI and QEESI are easy to administer. The QEESI requires only 10–15 min to complete. Obtaining the same amount of information through an interview would require considerably more time. The 0–10 rating scales are straightforward and quickly comprehended, and the 0–100 scale totals, readily interpretable. The scales measure dimensions widely viewed as relevant for assessing chemical sensitivity. Investigators can easily apply the cutoffs for symptoms (≥ 40), chemical intolerance (≥ 40), and other intolerance (≥ 25) to identify persons likely to be chemically sensitive, and the low cutoffs for the same scales to identify control subjects. Alternatively, researchers can apply the multiple logistic prediction equation provided here for subject selection. The calculations are easily done with a computer and possible with a calculator.

The findings of this study, while significant, should be interpreted with caution. First, the EESI and QEESI, like most clinical survey instruments, rely upon information that is both self-reported and retrospective. Patients are asked to recall symptoms and exposures that could span their entire lifetimes, given that adverse reactions to drugs and other substances may have occurred at any time. We did not interview or examine these patients or review their medical charts to determine what other illnesses or psychological profiles they might have had.

With respect to the large differences between patients and controls in scores on most of the items and all of the scales, it is possible that exposed groups are inclined to overreport their symptoms and intolerances. Although we did not perform serial or repeat measures to estimate test–retest reliability, in theory, the reliability would be the same as Cronbach's alpha reliability. Carmines and Zeller (1979) argue that Cronbach's alpha reliability is conservative and well-recommended for assessing scale reliability.

Items on the EESI and QEESI assess severity of responses to exposures, but they do not measure the frequency of those responses. Adding further questions to assess frequency would not only lengthen the instruments and administration time, but also might underestimate the importance of exposures for individuals who deliberately may be avoiding triggers and thus may be having infrequent adverse responses.

Potential uses for the EESI include the following.

(1) Selection of chemically sensitive subjects and controls for research studies involving chemical sensitivity. Optimally, subjects designated as being chemically sensitive should have high scores on the Symptom Severity (≥ 40), Chemical Intolerance (≥ 40), and Other Intolerance (≥ 25) scales; controls should have scores less than half of these levels, as shown in Table 8. In all cases, the lower the masking score, the greater the investigator's confidence that the classification is correct (for an analysis of the effect of masking, see Miller and Prihoda, 1999).

(2) Comparing putatively chemically sensitive populations studied by different investigators or specialists, e.g., patients seen by allergists, occupational medicine physicians, and psychiatrists.

(3) Assessment of chemical sensitivity in other study populations, e.g., patients with implants, chronic fatigue syndrome, or asthma, Gulf War veterans, or the general population.

(4) Following individual patients or groups of patients over time to evaluate the efficacy of therapies, such as exposure avoidance, medications, and psychotherapy. The QEESI's 50 items lend themselves to serial administration, e.g., annually, or pre- and post-intervention, to monitor progress.

(5) Clinical assessment of complex patients with intolerances by practitioners who face time constraints or who may be uncertain what questions to ask. Physicians may find it time-saving to provide the questionnaire to patients in advance of their appointments.

(6) Teaching medical students and residents how to evaluate patients for chemical sensitivity by providing a more uniform, quantitative measure than the current hodgepodge of clinical approaches. If routinely used by medical students and residents, this tool could enhance their competence in evaluating patients with chemical sensitivities.

As a cautionary note, although the EESI and QEESI have utility both as research and clinical tools, further confirmation of their validity and reliability by investigators in a variety of settings is needed. The sensitivity and specificity of these scales in other groups should be determined. Researchers and clinicians also need to be aware that scores on some scales may be low in chemically sensitive patients who are in the early stages of illness, who are masked (e.g., those who smoke or use steroids), or who have regained tolerance after months or years of avoiding exposures that trigger symptoms.

Conclusion

The EESI and QEESI offer investigators new tools for assessing chemical sensitivity along relevant dimensions. Screening questionnaires often demand that respondents make 'black and white' choices—e.g., sensitive or not—amid limitless shades of gray. The five scales described here allow investigators and clinicians to differentiate these shades. The single numerical ratings for each scale are readily interpretable, and the cutoff points offered here, easily applied. This new tool allows researchers to select study subjects with greater confidence, follow patients over time, gauge the effectiveness of therapeutic interventions, and compare findings with those of other investigators who use these scales.



Acknowledgments

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QEESI

This questionnaire is designed to facilitate history-taking from individuals who report chemical intolerances and for research on multiple chemical sensitivity (MCS) and the role of chemical intolerances in other conditions. It enables researchers and clinicians to characterize individuals along the dimensions most frequently reported as being associated with this health problem. The QEESI© contains four scales: Symptom Severity (scored 0–100), Chemical (Inhalant) Intolerances (0–100), Other Intolerances (0–100), and Life Impact (0–100). In addition, it contains a fifth scale, or Masking Index (0–10), that offers some assessment of ongoing exposures that may affect individuals' awareness of their intolerances and the intensity of their responses to environmental exposures.

Potential uses of the QEESI© include the following:

(1) In research studies, to facilitate characterization and cross-comparison of study populations.

(2) In clinical settings, to obtain a profile of patients' self-reported symptoms and intolerances. In certain cases, health professionals may wish to have patients complete a QEESI© at intervals in order to follow the course of their patients' symptoms and intolerances over time or in response to an intervention.

(3) In other settings, to provide individuals who report new intolerances with a questionnaire that they can fill out and then discuss with their personal physicians.

For persons who report that their symptoms began or became worse following a particular exposure, such as to pesticides or indoor air contaminants, the QEESI©'s four scales may be completed once in one color of ink, in order to show self-reported responses before the event, and a second time in another color to show responses since the event. A special feature of the QEESI© is the 'Symptom Star' which provides a visual representation of the person's responses on the Symptom Severity scale. The Symptom Star can also be completed for both pre- and post-exposure symptoms.

For additional copies of the QEESI©, contact Claudia S. Miller, M.D., M.S., University of Texas Health Science

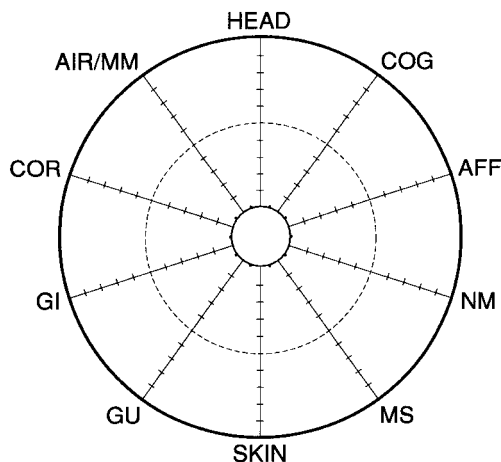
Center at San Antonio, Department of Family Practice, Suite 610-L, 7703 Floyd Curl Drive, San Antonio, Texas 78284-7794. For further information, see *Chemical Exposures: Low Levels and High Stakes* by Nicholas A. Ashford and Claudia S. Miller, John Wiley and Sons, New York, NY 1998.

Key: HEAD=head-related symptoms; COG=cognitive symptoms; AFF= affective symptoms; NM=neuromuscular symptoms; MS=musculoskeletal symptoms; SKIN=skin-related symptoms; GU=genitourinary symptoms; GI=gastrointestinal symptoms; COR=heart/chest-related symptoms; AIR/MM=airway or mucous membrane-related symptoms.

QUICK ENVIRONMENTAL EXPOSURE AND SENSITIVITY INVENTORY V-1 (QEESI)©

The purpose of this questionnaire is to help identify health problems you may be having and to understand your responses to various exposures. If your health problems began suddenly or became much worse after a particular exposure event, such as a pesticide exposure or moving to a new home or office building, complete pages 1-3 describing how you are now, then go back through these same questions a second time, and identify how you were before the exposure event. After you have completed all of the items on pages 1-5, fill in the "target" diagram below.

SYMPTOM STAR



Instructions: After completing pages 1 through 5, unfold page 3 so that it lies just to the right of this page. Place a small dot on the corresponding spoke for each symptom item on page 3. Connect these points. For "before and after" scores (described above), use two different colors.



CHEMICAL EXPOSURES

The following items ask about your responses to various odors or chemical exposures. Please indicate whether or not these odors or exposures would make you feel sick, for example, you would get a headache, have difficulty thinking, feel weak, have trouble breathing, get an upset stomach, feel dizzy, or something like that. For any exposure that makes you feel sick, on a 0-10 scale rate the severity of your symptoms with that exposure. For exposures that do not bother you, answer "0." Do not leave any items blank.

0 = not at all a problem
5 = moderate symptoms
10 = disabling symptoms

For each item, circle one number only:

1. Diesel or gas engine exhaust	0 1 2 3 4 5 6 7 8 9 10
2. Tobacco smoke	0 1 2 3 4 5 6 7 8 9 10
3. Insecticide	0 1 2 3 4 5 6 7 8 9 10
4. Gasoline, for example at a service station while filling the gas tank	0 1 2 3 4 5 6 7 8 9 10
5. Paint or paint thinner	0 1 2 3 4 5 6 7 8 9 10
6. Cleaning products such as disinfectants, bleach, bathroom cleansers or floor cleaners	0 1 2 3 4 5 6 7 8 9 10
7. Certain perfumes, air fresheners or other fragrances	0 1 2 3 4 5 6 7 8 9 10
8. Fresh tar or asphalt	0 1 2 3 4 5 6 7 8 9 10
9. Nailpolish, nailpolish remover, or hairspray	0 1 2 3 4 5 6 7 8 9 10
10. New furnishings such as new carpeting, a new soft plastic shower curtain or the interior of a new car	0 1 2 3 4 5 6 7 8 9 10

Total Chemical Intolerance Score (0-100):

Name any additional chemical exposures that make you feel ill and score them from 0 to 10: _____

OTHER EXPOSURES

The following items ask about your responses to a variety of other exposures. As before, please indicate whether these exposures would make you feel sick. Rate the severity of your symptoms on a 0-10 scale. Do not leave any items blank.

0 = not at all a problem
5 = moderate symptoms
10 = disabling symptoms

For each item, circle one number only:

1. Chlorinated tap water	0 1 2 3 4 5 6 7 8 9 10
2. Particular foods, such as candy, pizza, milk, fatty foods, meats, barbecue, onions, garlic, spicy foods, or food additives such as MSG	0 1 2 3 4 5 6 7 8 9 10
3. Unusual cravings, or eating any foods as though you were addicted to them; or feeling ill if you miss a meal	0 1 2 3 4 5 6 7 8 9 10
4. Feeling ill after meals	0 1 2 3 4 5 6 7 8 9 10
5. Caffeine, such as coffee, tea, Snapple, cola drinks, Big Red, Dr. Pepper or Mountain Dew, or chocolate	0 1 2 3 4 5 6 7 8 9 10
6. Feeling ill if you drink or eat less than your usual amount of coffee, tea, caffeinated soda or chocolate, or miss it altogether	0 1 2 3 4 5 6 7 8 9 10
7. Alcoholic beverages in small amounts such as one beer or a glass of wine	0 1 2 3 4 5 6 7 8 9 10
8. Fabrics, metal jewelry, creams, cosmetics, or other items that touch your skin	0 1 2 3 4 5 6 7 8 9 10
9. Being unable to tolerate or having adverse or allergic reactions to any drugs or medications (such as antibiotics, anesthetics, pain relievers, x-ray contrast dye, vaccines or birth control pills), or to an implant, prosthesis, contraceptive chemical or device, or other medical, surgical or dental material or procedure	0 1 2 3 4 5 6 7 8 9 10
10. Problems with any classical allergic reactions (asthma, nasal symptoms, hives, anaphylaxis or eczema) when exposed to allergens such as: tree, grass or weed pollen, dust, mold, animal dander, insect stings or particular foods	0 1 2 3 4 5 6 7 8 9 10

Total Other Intolerance Score (0-100):



SYMPTOMS

The following questions ask about symptoms you may have experienced commonly. Rate the severity of your symptoms on a 0-10 scale. Do not leave any items blank.

0 = not at all a problem
 5 = moderate symptoms
 10 = disabling symptoms

For each item, circle one number only:

1	Problems with your muscles or joints, such as pain, aching, cramping, stiffness or weakness?	MS 0 1 2 3 4 5 6 7 8 9 10
2	Problems with burning or irritation of your eyes, or problems with your airway or breathing, such as feeling short of breath, coughing, or having a lot of mucus, post-nasal drainage, or respiratory infections?	AIR/MM 0 1 2 3 4 5 6 7 8 9 10
3	Problems with your heart or chest, such as a fast or irregular heart rate, skipped beats, your heart pounding, or chest discomfort?	COR 0 1 2 3 4 5 6 7 8 9 10
4	Problems with your stomach or digestive tract, such as abdominal pain or cramping, abdominal swelling or bloating, nausea, diarrhea, or constipation?	GI 0 1 2 3 4 5 6 7 8 9 10
5	Problems with your ability to think, such as difficulty concentrating or remembering things, feeling spacey, or having trouble making decisions?	COG 0 1 2 3 4 5 6 7 8 9 10
6	Problems with your mood, such as feeling tense or nervous, irritable, depressed, having spells of crying or rage, or loss of motivation to do things that used to interest you?	AFF 0 1 2 3 4 5 6 7 8 9 10
7	Problems with balance or coordination, with numbness or tingling in your extremities, or with focusing your eyes?	NM 0 1 2 3 4 5 6 7 8 9 10
8	Problems with your head, such as headaches or a feeling of pressure or fullness in your face or head?	HEAD 0 1 2 3 4 5 6 7 8 9 10
9	Problems with your skin, such as a rash, hives or dry skin?	SKIN 0 1 2 3 4 5 6 7 8 9 10
10	Problems with your urinary tract or genitals, such as pelvic pain or frequent or urgent urination? (For women: or discomfort or other problems with your menstrual period?)	GU 0 1 2 3 4 5 6 7 8 9 10

Total Symptom Score (0-100):

MASKING INDEX

The following items refer to ongoing exposures you may be having. Circle "0" if the answer is NO, or if you don't know whether you have the exposure. Circle "1" if the answer is YES, you do have the exposure. Do not leave any items blank.

Circle "0" or "1" only:

1.	Do you smoke or dip tobacco once a week or more often?	NO=0 YES=1
2.	Do you drink any alcoholic beverages, beer, or wine once a week or more often?	NO=0 YES=1
3.	Do you consume any caffeinated beverages once a week or more often?	NO=0 YES=1
4.	Do you routinely (once a week or more) use perfume, hairspray, or other scented personal care products?	NO=0 YES=1
5.	Has either your home or your workplace been sprayed for insects or fumigated in the past year?	NO=0 YES=1
6.	In your current job or hobby, are you routinely (once a week or more) exposed to any chemicals, smoke or fumes?	NO=0 YES=1
7.	Other than yourself, does anyone routinely smoke inside your home?	NO=0 YES=1
8.	Is either a gas or propane stove used for cooking in your home?	NO=0 YES=1
9.	Is a scented fabric softener (liquid or dryer sheet) routinely used in laundering your clothes or bedding?	NO=0 YES=1
10.	Do you routinely (once a week or more) take any of the following: steroid pills, such as prednisone; pain medications requiring a prescription; medications for depression, anxiety, or mood disorders; medications for sleep; or recreational or street drugs?	NO=0 YES=1

Masking Index (0-10):
 (Total number of YES answers)



IMPACT OF SENSITIVITIES

If you are sensitive to certain chemicals or foods, on a scale of 0-10 rate the degree to which your sensitivities have affected various aspects of your life. If you are not sensitive or if your sensitivities do not affect these aspects of your life, answer "0." Do not leave any items blank.

0 = not at all
5 = moderately
10 = severely

How much have your sensitivities affected:

1. Your diet	0 1 2 3 4 5 6 7 8 9 10
2. Your ability to work or go to school	0 1 2 3 4 5 6 7 8 9 10
3. How you furnish your home	0 1 2 3 4 5 6 7 8 9 10
4. Your choice of clothing	0 1 2 3 4 5 6 7 8 9 10
5. Your ability to travel to other cities or drive a car	0 1 2 3 4 5 6 7 8 9 10
6. Your choice of personal care products, such as deodorants or makeup	0 1 2 3 4 5 6 7 8 9 10
7. Your ability to be around others and enjoy social activities, for example, going to meetings, church, restaurants, etc.	0 1 2 3 4 5 6 7 8 9 10
8. Your choice of hobbies or recreation	0 1 2 3 4 5 6 7 8 9 10
9. Your relationship with your spouse or family	0 1 2 3 4 5 6 7 8 9 10
10. Your ability to clean your home, iron, mow the lawn, or perform other routine chores	0 1 2 3 4 5 6 7 8 9 10

Total Life Impact Score (0-100):

For additional copies of the QEESI, call 210-567-7760. For more information about this questionnaire, refer to Chemical Exposures: Low Levels and High Stakes (2nd Edition) by Nicholas A. Ashford and Claudia S. Miller, John Wiley & Sons, Inc., 1998.

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