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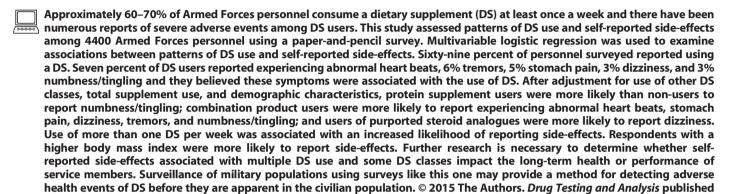
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# Self-reported side-effects associated with use of dietary supplements in an armed forces population

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# Introduction

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Approximately 60–70% of Armed Forces personnel use a dietary supplement (DS) at least once a week.<sup>[1]</sup> Use of multiple supplements is prevalent among military personnel with 22% reporting the use of 3 or more DS per week.<sup>[2]</sup> Use of DS by civilians is lower with 44–53% reporting use of at least one DS per week and approximately 10% stating they use 5 or more DS per week.<sup>[3]</sup> Military service members use more products marketed for their ability to enhance performance than civilians, which has been attributed to extensive work-related emphasis on physical fitness and mental readiness.<sup>[2]</sup>

Multiple reports have documented severe adverse health events in Armed Forces personnel attributed to use of single and multiple DS, including the consumption of DS that contain high doses of various stimulants such as ephedra and 1,3-dimethylamylamine (DMAA). [4–8] Only serious adverse health events resulting from DS use must be reported by DS manufacturers to the US Food and Drug Administration (FDA) and there is no requirement to report minor adverse health events. [9] It is estimated that only 1 in 100 adverse events associated with DS use are reported to the FDA. [10] As a result, minimal data documenting associations of relatively minor adverse health events with DS use are available. [111,12] It is widely recognized that in the USA current procedures for identifying and withdrawing dangerous DS are inadequate. [13] In 2008, the Institutes of Medicine (IOM) Committee on Dietary Supplement Use by Military Personnel stated there was a critical requirement

to identify potentially harmful effects of DS that may compromise the health and performance of service members. [14] Although extensive data on DS use are collected in national nutrition surveys, such as the National Health and Nutrition Examination Survey (NHANES), the association between DS and self-reported side-effects is not typically assessed. For most service members, there is no official policy on supplement use and personnel are able to utilize supplements at their discretion. Given the widespread availability of DS at military exchanges and General Nutrition Centers located on military installations and the Internet, this investigation examined patterns of DS use and demographic factors associated with self-reported side-effects in over 4000 uniformed service members.

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supplement and included the Supplement

Dietary supplement that included one or

more herbal ingredients with no nutrients or

other supplement ingredients; also includes

# **Methods**

# **Participants**

This study was approved by the Human Use Review Committee at the US Army Research Institute of Environmental Medicine. In 2010-2011, a convenience sample of 1207 Army, 1787 Air Force, 1059 Coast Guard, and 483 deployed uniformed service members completed the survey. After exclusion of 96 surveys due to missing data, the final sample consisted of 4440 military and Coast Guard personnel. The sample was collected at 12 Army (10 US installations and 2 overseas sites), 8 Air Force (7 US installations and 1 overseas site) and 13 Coast Guard bases (all US installations). Deployed personnel stationed in various regions of Iraq or Afghanistan also participated. Users and non-users of DS were included in the sample. Healthcare professionals recruited participants and no incentives were offered for completion of the survey. The healthcare professional worked with unit commanders to arrange a time and place to distribute the survey in person in a classroom setting. A standardized presentation describing the purpose of the study, survey contents, and procedures for completing it were provided to potential participants. Participants completed the survey after an explanation that all information obtained would remain confidential and that participation was voluntary. Investigators adhered to US Army Regulation 70-25 and US Army Medical Research and Materiel Command Regulation 70-25 on the use of volunteers in research.[15]

#### Survey

Development of the survey used in the present study, the Dietary Supplement Survey of US Army Active Duty Personnel, has been described elsewhere. [2,16] Service specific questions on the original Army survey, pertaining, for example to rank, were modified as necessary. The questionnaire used to conduct the initial Army survey can be found in the Supporting information. The estimated response rate of individuals asked to participate in the study was 80%. The survey consisted of 43 total questions, of which 15 directly assessed the use of DS. One multipart question asked participants about self-reported side-effects related to their use of any DS, including abnormal rapid heart rate, stomach pain, dizziness, tremors, or numbness/tingling, and loss of consciousness. A space for participants to write-in unspecified 'other' side-effects was also included. Side-effects chosen for inclusion were based on a review of the available research literature when the survey was initially formulated (2006) regarding self-reported side-effects from DS use. Participants were also asked about demographic characteristics and type and frequency of DS used. Ninety-two individual supplements were listed in the survey including 55 generic supplements such as multivitamins, individual vitamins and minerals, combination antioxidants, and 37 brand-named products. Participants were instructed to write in DS used that were not on the survey. Selection of branded DS for inclusion was based on then-current patterns of DS purchases at Armed Forces exchange systems and General Nutrition Center stores on or near military installations. Prior to data analyses, individual supplement and supplement types were grouped into the following categories by research staff (Table 1): multivitamin and mineral, individual vitamin and mineral, protein/amino acid supplement, combination product, herbal supplement, purported steroid analogue and 'other'. Respondents reporting the use of a DS at least once per week in the six months prior to the survey were classified as DS users. Total weekly

Table 1. Dietary supplement categories derived from the Dietary Supplement and Caffeine Intake Survey of U.S. Army Active Duty Personnel Definition Category **Dietary Supplement** Any dietary supplement as defined by the DSHEA<sup>a</sup> legislation. Multivitamin and Dietary supplement containing two or more vitamins or minerals and no additional mineral supplement ingredients. **Individual Vitamins** Dietary supplement that were single nutrient or Minerals ingredient supplements, such as calcium or vitamin D. Protein and Amino Amino acid mixtures, protein powders, and Acid similar products in which the intention is to provide a single or complex protein source. **Combination Products** Dietary supplement with mixtures of ingredients from any of the above categories; included two or more categories and multiple ingredients. Purported Steroid Steroidal hormones or herbal substitutes for **Analogues** hormones that were marketed as dietary

<sup>a</sup>DSHEA, Dietary Supplement Health and Education Act.

supplement use was determined by summing the number of unique supplements reported by a participant to be used at least once per week.

Facts panel on the label.

plant-derived ingredients.

#### **Data analyses**

**Herbal Supplements** 

Completed surveys were scanned using ScanTools Plus with ScanFlex (version 6.301; Scantron Corporation, Eagan, MN, USA) and data were imported into SPSS (version 20.0; SPSS Inc, Chicago, IL, USA) for conversion to a SAS (version 9.2; SAS Institute, Cary, NC, USA) data file for all statistical analyses. Descriptive statistics, including means and standard deviations (SD), as well as percentages of demographic characteristics, DS use, and side-effects were determined using the proc means and proc freq procedures. Logistic regression was performed using the survey logistic procedure to examine associations between: (1) demographic characteristics and DS use; (2) demographic characteristics and self-reported side-effects; (3) total DS use and self-reported side-effects; and (4) classes of DS use and self-reported side-effects. Associations are presented for all models as odds ratios (OR) and 95% confidence intervals (CI). Models examining associations between total DS use and self-reported side-effects were adjusted for demographic characteristics (gender, education, BMI, age, aerobic exercise, and branch). Models examining classes of DS use and self-reported side-effects were adjusted for other classes of DS use, total DS use, and demographic characteristics (gender, education, BMI, age, aerobic exercise, and branch). To adjust for other classes of DS use, each class of DS use was included in the model (multivitamin and mineral, individual vitamin or mineral, protein supplement, combination product, herbal, steroid, or other).

# **Results and discussion**

Eighty percent of the participants in the present study were male and 20% female, similar to the representation of these groups in the uniformed services surveyed. The average (mean  $\pm$  SD) age was 28.6  $\pm$  7.4 years and BMI was 26.5  $\pm$  3.8. Twenty-five percent of participants reported having some high school education, 55% some college or an associate degree, and 20% a Bachelor or graduate degree. Sixty-nine percent of participants reported using a DS ≥ 1 time/week for the 6 months prior to the survey. Thirty-three percent used 1-2 DS at least once per week, 17% used 3-4 supplements per week and 23% reported using 5 or more DS at least once per week. Forty-four percent of participants consumed a multivitamin and mineral, 32% a protein supplement, 25% combination products, 22% an individual vitamin or mineral, 21% consumed a DS classified as 'other', 8% a herbal supplement, and 1% a supplement classified as a steroid analogue at least once a week. Seven percent of DS users reported experiencing abnormal heart beats, 6% tremors, 5% stomach pain, 3% dizziness, and 3% numbness and/or tingling that was associated with DS use. Loss of consciousness was not included in further analyses because prevalence (0.12 %) was too low for association analyses to be performed.

#### Demographic characteristics and DS use

Associations between demographic characteristics and DS use are presented in Table 2. Female personnel were more likely than males to use multivitamin and minerals or individual vitamin or mineral DS and less likely to use protein or combination products. Participants reporting some college or a Bachelor or graduate degree were more likely than respondents with at least some high school to use multivitamins and minerals, individual vitamins or minerals, or products classified as 'other'. Respondents reporting some college education were also more likely than those with at least some high school graduates to use protein supplements. Those with an advanced degree were less likely than high school graduates to use combination products. Those with a body mass index (BMI) of 25.0–29.9 were more likely than those with a BMI of 18-24.9 to use multivitamins and minerals, combination products, purported steroid analogues, and products classified as 'other'. Those with a BMI of ≥30 were more likely than those with a BMI of 18–24.9 to use combination products, but less likely to use protein supplements. Participants aged ≥25 years of age were more likely than those 18-24 years to use multivitamins and minerals and 'other' DS. Participants aged >40 years were more likely than those 18-24 years to use individual vitamin or minerals and less likely to use protein supplements and combination products. Those who engaged in at least 61 min or more per week of aerobic exercise were more likely than those who engaged in 0-60 min to use a multivitamin and mineral or protein DS. Respondents who engaged in 465 min or more per week were more likely than those who engaged in 0-60 min to use individual vitamins or minerals. Participants who engaged in 315 or more min of aerobic exercise per week were more likely than those who engaged in 0-60 min to use combination products and other DS.

# Demographic characteristics and self-reported side-effects

Associations between demographic characteristics and self-reported side-effects are presented in Table 3. Male respondents were more likely to report experiencing dizziness than females. Participants with some college education were more likely than respondents with at least some high school education to report stomach

pain. Personnel with a BMI of  $\geq$ 30 were more likely than those with a BMI of 18–24.9 to report abnormal heart beats, stomach pain, dizziness, and tremors. Those with a BMI of 25.0–29.9 were also more likely than those with a BMI of 18–24.9 to report tremors. Participants aged  $\geq$ 40 years were less likely than those aged 18–24 years to report experiencing numbness or tingling.

#### Total supplement use and self-reported side-effects

Associations between total supplement use and self-reported side-effects, adjusted for demographic characteristics of branch, sex, age, education, BMI, and participation in aerobic exercise are presented in Table 4. After adjustment, those using 1–2 DS per week were one-and-a-half times more likely than non-users to report abnormal heart beats and those using 3–4 or 5 or more DS per week were over three times more likely than non-users to report abnormal heart beats. Those using 3–4 or 5 or more DS per week were also two to three times more likely than non-users to report stomach pain, dizziness tremors, and numbness/tingling.

#### Classes of DS use and self-reported side-effects

Crude associations between classes of DS use and self-reported side-effects, as well as models adjusted for: (1) use of other DS classes; (2) total supplement use; and (3) use of other DS classes, total supplement use, and demographic characteristics are presented in Table 5. After adjustment for total supplement use, use of other DS classes and demographic characteristics, users of protein supplements were two and a half times more likely than non-users to experience numbness/tingling. Combination product users were two to more than three and a half times more likely to self-report experiencing abnormal heart beats, stomach pain, dizziness, tremors, and numbness/tingling. Users of purported steroid analogues were more than two and a half times more likely than non-users to report experiencing dizziness. All other significant associations identified in crude models were attenuated after adjustment.

The findings of the present study are in agreement with previous reports documenting associations between DS use and a variety of self-reported side-effects in DS users. [17,18] Overall self-reported prevalence of perceived side-effects from DS use was greater among military personnel than previously found by Chiba et al.[17] (24% vs. 3%) for civilians and significantly greater than the 1% reported by current FDA reporting systems for the civilian population.[11] The association among military personnel was related to the number of unique supplements used by respondents; as the number of DS used increased, so did self-reported side-effects. In addition, after adjustment for use of other DS classes, total supplement use, and demographic characteristics, users of protein supplements were more likely to report numbness/tingling, combination product users were more likely to report abnormal heart beats, stomach pain, dizziness, tremors and numbness/tingling, and users of purported steroid analogue DS were more likely to report dizziness.

The association between total supplement use and side-effects, as well as between combination product use and side-effects identified in the present study, is in agreement with clinical case reports of severe adverse events resulting from multiple supplement use and causality assessments in patients presenting with acute liver injury attributed to concurrent use of multiple supplements, including combination products, as well as numerous other reports in the literature. We identified BMI as a demographic characteristic associated with increased use of both combination product and several self-reported side-effects. The increased use of combination

Table 2.         Associations between demographic characteristics and dietary supplement use	ographic characteristic	s and dietary supplement u	Ise				
Demographic Characteristic			Die	Dietary Supplement Class			
	Multivitamin (OR,95% CI) <sup>a</sup>	Individual Vitamin or Mineral (OR,95% CI)	Protein Supplement (OR,95% CI)	Combination Products (OR,95% CI)	Herbal (OR,95% CI)	Steroid (OR,95% CI)	Other (OR,95% CI)
Gender							
Male	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Female	1.33 (1.15, 1.55)	2.08 (1.77, 2.45)	0.33 (0.27, 0.40)	0.49 (0.41, 0.60)	1.02 (0.77, 1.35)	0.45 (0.19, 1.05)	1.13 (0.95, 1.35)
Education							
Some High School/High School	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Some College	1.66 (1.43, 1.93)	1.30 (1.09, 1.56)	1.20 (1.03, 1.40)	1.11 (0.94, 1.31)	1.29 (0.97, 1.71)	0.76 (0.43, 1.35)	1.79 (1.47, 2.18)
Bachelor/Graduate Degree	2.47 (2.05, 2.96)	1.62 (1.31, 2.00)	1.16 (0.96, 1.40)	0.69 (0.55, 0.85)	1.09 (0.77, 1.55)	0.52 (0.23, 1.19)	2.38 (1.90, 2.98)
Body Mass Index							
≤18-24.9	1.0	1.0	1.0	1.0	1.0	1.0	1.0
25.0-29.9	1.22 (1.07, 1.39)	0.98 (0.84, 1.15)	1.08 (0.94, 1.24)	1.31 (1.12, 1.54)	1.05 (0.82, 1.35)	2.08 (1.10, 3.92)	1.31 (1.12, 1.54)
30+	1.02 (0.86, 1.22)	0.96 (0.78, 1.18)	0.72 (0.59, 0.88)	1.60 (1.31, 1.94)	0.99 (0.71, 1.38)	1.37 (0.58, 3.23)	0.96 (0.77, 1.20)
Age (years)							
18-24	1.0	1.0	1.0	1.0	1.0	1.0	1.0
25-29	1.78 (1.53, 2.08)	0.99 (0.83, 1.19)	1.11 (0.95, 1.29)	1.03 (0.88, 1.22)	1.04 (0.78, 1.37)	1.23 (0.65, 2.33)	1.38 (1.14, 1.66)
30-39	1.77 (1.51, 2.07)	0.98 (0.81, 1.18)	0.76 (0.65, 0.90)	0.85 (0.71, 1.01)	1.04 (0.78, 1.39)	1.01 (0.51, 2.03)	1.37 (1.13, 1.67)
40+	2.24 (1.81, 2.77)	1.38 (1.08, 1.75)	0.50 (0.39, 0.65)	0.43 (0.32, 0.58)	0.95 (0.63, 1.44)	1.31 (0.55, 3.14)	2.20 (1.73, 2.80)
Aerobic Exercise (minutes)							
09-0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
61-314	1.67 (1.29, 2.15)	1.12 (0.83, 1.52)	1.36 (1.03, 1.80)	1.31 (0.96, 1.78)	1.03 (0.65, 1.65)	1.11 (0.33, 3.68)	1.21 (0.88, 1.65)
315-464	1.69 (1.29, 2.23)	1.33 (0.96, 1.84)	1.62 (1.20, 2.19)	1.74 (1.25, 2.42)	1.09 (0.66, 1.82)	1.44 (0.41, 5.09)	1.45 (1.04, 2.02)
465 or more	2.05 (1.55, 2.73)	1.52 (1.09, 2.12)	2.83 (2.09, 3.84)	2.64 (1.90, 3.68)	1.33 (0.80, 2.22)	2.30 (0.67, 7.97)	1.51 (1.07, 2.12)
<sup>a</sup> OR/95% Cl, Odds Ratio, 95% Confidence Interval	ence Interval.						

			Side-effects		
	Abnormal Heart Beats (OR, 95% CI) <sup>a</sup>	Stomach Pain (OR, 95% CI)	Dizziness (OR, 95% CI)	Tremors (OR, 95% CI)	Numbness/ Tingling (OR, 95% CI)
Gender					
Female	1.0	1.0	1.0	1.0	1.0
Male	1.24 (0.94, 1.63)	1.21 (0.88, 1.69)	1.53 (1.06, 2.22)	1.26 (0.94, 1.70)	0.63 (0.38, 1.07)
Education					
Some High School/High School	1.0	1.0	1.0	1.0	1.0
Some College	1.13 (0.85, 1.49)	1.52 (1.06, 2.18)	1.12 (0.74, 1.67)	1.12 (0.83, 1.52)	0.99 (0.65, 1.51)
Bachelor/Graduate Degree	0.88 (0.61, 1.27)	1.29 (0.83, 2.01)	1.06 (0.64, 1.76)	0.78 (0.52, 1.17)	0.67 (0.38, 1.20)
Body Mass Index					
≤18-24.9	1.0	1.0	1.0	1.0	1.0
25.0-29.9	1.21 (0.92, 1.60)	0.86 (0.62, 1.18)	1.13 (0.77, 1.67)	1.51 (1.11, 2.05)	0.87 (0.59, 1.29)
30+	1.91 (1.38, 2.63)	1.52 (1.06, 2.19)	1.69 (1.08, 2.65)	2.00 (1.39, 2.86)	0.80 (0.46, 1.36)
Age (years)					
18–24	1.0	1.0	1.0	1.0	1.0
25–29	1.25 (0.94, 1.65)	1.17 (0.85, 1.62)	0.79 (0.53, 1.18)	1.24 (0.91, 1.69)	1.01 (0.67, 1.53)
30–39	1.07 (0.79, 1.45)	0.76 (0.52, 1.10)	0.67 (0.43, 1.03)	1.04 (0.75, 1.45)	0.69 (0.43, 1.12)
40+	0.60 (0.36, 1.01)	0.62 (0.35, 1.10)	0.61 (0.32, 1.17)	0.82 (0.50, 1.34)	0.27 (0.10, 0.76)
Aerobic Exercise(minutes)					
0 –60	1.0	1.0	1.0	1.0	1.0
61–314	0.75 (0.49, 1.17)	0.78 (0.46, 1.32)	0.82 (0.43, 1.57)	0.93 (0.56, 1.55)	0.75 (0.37, 1.53)
315–464	0.86 (0.30, 1.40)	0.95 (0.54, 1.68)	1.02 (0.51, 2.05)	1.07 (0.62, 1.85)	1.18 (0.56, 2.51)
465 or more	0.97 (0.59, 1.58)	0.92 (0.51, 1.67)	1.05 (0.51, 2.14)	1.05 (0.59, 1.84)	1.29 (0.60, 2.78)

Side-effects		Total Suppler	ment Use	
	None	1-2 (OR, 95% CI) <sup>a</sup>	3-4(OR, 95% CI)	≥5(OR, 95% CI)
Abnormal Heart Beats				
% (SE)	3.4 (0.52)	5.3 (0.58)	9.7 (1.09)	11.5 (1.01)
OR (95% CI) <sup>b</sup>	1.0	1.58 (1.07, 2.34)	3.35 (2.23, 5.03)	3.86 (2.65, 5.63)
Stomach Pain				
% (SE)	2.8 (0.48)	3.5 (0.48)	5.5 (0.84)	8.6 (0.89)
OR (95% CI) <sup>b</sup>	1.0	1.25 (0.80, 1.96)	2.15 (1.35, 3.44)	3.28 (2.18, 4.94)
Dizziness				
% (SE)	2.1 (0.41)	2.5 (0.40)	3.9 (0.71)	5.6 (0.73)
OR (95% CI) <sup>b</sup>	1.0	1.19 (0.70, 2.02)	2.11 (1.20, 3.72)	2.99 (1.83, 4.90)
Tremors				
% (SE)	3.2 (0.50)	4.6 (0.54)	8.8 (1.04)	8.8 (0.90)
OR (95% CI) <sup>b</sup>	1.0	1.44 (0.95, 2.18)	3.12 (2.05, 4.74)	3.05 (2.05, 4.54)
Numbness/Tingling				
% (SE)	1.2 (0.31)	1.4 (0.30)	3.5 (0.68)	6.3 (0.77)
OR (95% CI) <sup>b</sup>	1.0	1.28 (0.64, 2.57)	3.35 (1.72, 6.53)	5.88 (3.22, 10.71)

<sup>&</sup>lt;sup>a</sup>OR/95% CI, Odds Ratio, 95% Confidence Interval.

products by those with a BMI >30 is in agreement with a report by Cohen<sup>[18]</sup> in which civilians using a combination product intended to promote weight loss, especially those who were obese, also reported a high prevalence of self-reported side-effects, including dry mouth, insomnia, and anxiety.

Increased BMI has been demonstrated to negatively affect cardiometabolic risk and is associated with increased mortality. [23] Consistent with reports from the civilian literature, the present study identified a greater association of specific self-reported side-effects in military personnel reporting a BMI of ≥30. These respondents were also more likely to use combination products, which raises concern given the increased cardiometabolic risk profile in this population. Additional demographic predictors of combination product use included a BMI of 25-29.9 and participation in aerobic exercise of long duration; however, these characteristics were not associated with an increased likelihood of

<sup>&</sup>lt;sup>b</sup>Adjusted for age, gender, education, aerobic exercise, body mass index, and branch.

Lyser, Cl. <sup>1</sup> Metalista (Apparation of Proteins)         Provisionation of Apparation of Appa	Multivitamin   Individual Vitamin or   Protein   Protein   Combination   Protein   P						Supplement Class	III CIdss							
Monetal   Mone	Signature   User   Nor-user   User   U		Aultivitamin DR, 95% CI) <sup>a</sup>	Individua Mineral ((	Vitamin or JR, 95% CI)	Pro Supple (OR, 9	rtein ements 15% CI)	Comi Prc (OR,	bination oducts 95% CI)	He (OR, 9	rbals 95% CI)	Purport Ana (OR,	ed Steroid logues 95% Cl)	O(OR,	Other (OR, 95% CI)
5.2         9.1         6.5         8.4         5.6         9.6         4.5         14.0         6.7         17.3         1.0         0.39         1.1         6.7         0.39         0.39         1.0         0.39         1.1         0.39         1.1         0.39         1.1         0.38         1.0         0.38         1.0         0.39         1.0         0.34         1.0         0.39         1.0         0.39         1.0         0.39         1.0         0.39         1.0         1.39         1.0         0.39         1.0         1.38         1.0         1.39         1.0         1.39         1.0         1.38         1.0         1.39         1.0         1.39         1.0         1.38         1.0 </th <th>5.2 9.1 6.5 8.4 5.6 9.6 45  (0.44) (0.66) (0.42) (0.88) (0.42) (0.79) (0.36)  (1.45,232) (1.01,171) (1.42,227) (1.45,227)  (1.45,232) (1.01,171) (1.42,227) (1.02,271)  (1.45,232) (0.72,128) (0.72,128) (0.57,107)  (1.40,141) (0.89,162) (0.60,118) (0.65,108) (0.57,107)  (1.41,199) (0.54) (0.59) (0.57,113) (0.55,108)  (1.41,199) (0.57,113) (0.55,108) (0.55,108)  (1.41,199) (0.57,113) (0.55,108) (0.55,108)  (1.41,199) (0.65,118) (0.65,118) (0.55,108)  (1.41,199) (0.65,118) (0.65,118) (0.55,108)  (1.41,199) (0.65,118) (0.65,118) (0.65,118)  (1.41,199) (0.65,118) (0.65,118) (0.65,118)  (1.41,199) (0.65,118) (0.65,118) (0.65,118)  (1.41,199) (0.65,118) (0.65,118) (0.65,118)  (1.41,124) (0.65,118) (0.65,118) (0.65,118)  (1.41,125) (0.65,118) (0.65,118) (0.65,118)  (1.41,126) (0.65,118) (0.65,118) (0.65,118)  (1.42,127) (0.65,118) (0.65,118) (0.65,118)  (1.44,128) (0.65,11</th> <th></th> <th></th> <th>Non-user</th> <th>User</th> <th>Non-user</th> <th>User</th> <th>Non-user</th> <th>User</th> <th>Non-user</th> <th>User</th> <th>Non-user</th> <th>User</th> <th>Non-user</th> <th>User</th>	5.2 9.1 6.5 8.4 5.6 9.6 45  (0.44) (0.66) (0.42) (0.88) (0.42) (0.79) (0.36)  (1.45,232) (1.01,171) (1.42,227) (1.45,227)  (1.45,232) (1.01,171) (1.42,227) (1.02,271)  (1.45,232) (0.72,128) (0.72,128) (0.57,107)  (1.40,141) (0.89,162) (0.60,118) (0.65,108) (0.57,107)  (1.41,199) (0.54) (0.59) (0.57,113) (0.55,108)  (1.41,199) (0.57,113) (0.55,108) (0.55,108)  (1.41,199) (0.57,113) (0.55,108) (0.55,108)  (1.41,199) (0.65,118) (0.65,118) (0.55,108)  (1.41,199) (0.65,118) (0.65,118) (0.55,108)  (1.41,199) (0.65,118) (0.65,118) (0.65,118)  (1.41,199) (0.65,118) (0.65,118) (0.65,118)  (1.41,199) (0.65,118) (0.65,118) (0.65,118)  (1.41,199) (0.65,118) (0.65,118) (0.65,118)  (1.41,124) (0.65,118) (0.65,118) (0.65,118)  (1.41,125) (0.65,118) (0.65,118) (0.65,118)  (1.41,126) (0.65,118) (0.65,118) (0.65,118)  (1.42,127) (0.65,118) (0.65,118) (0.65,118)  (1.44,128) (0.65,11			Non-user	User	Non-user	User	Non-user	User	Non-user	User	Non-user	User	Non-user	User
5.2         9.1         6.5         8.4         5.6         9.6         4.5         14.0         6.5         12.1         6.7           Whodel 1°         (1.44)         (1.66)         (0.42)         (0.42)         (0.73)         (1.04)         (0.39)         (1.80)         (0.38)           Whodel 2°         (1.0         (1.33)         (1.01, 1.71)         (1.72, 2.27)         (2.71, 4.55)         (1.04)         (2.99)         (1.0         (3.44)         (1.0         (1.99)         (1.0         (3.89)         (1.00)         (3.89)         (1.00)         (3.89)         (1.00)         (3.89)         (1.00)         (3.89) </td <td>5.2 9.1 6.5 84 5.6 9.6 45  (0.44) (0.66) (0.42) (0.88) (0.42) (0.79) (0.36)  (0.44) (0.66) (0.42) (0.88) (0.42) (0.79) (0.36)  (1.45,2.23) (1.01,1.71) (1.42,2.27) (1.05,1.23)  (1.07,1.82) (0.09,1.8) (0.07,2.128) (0.57,1.07)  (0.91,1.61) (0.60,1.8) (0.65,1.07) (0.57,1.07)  (0.92,1.62) (0.93) (0.60,1.8) (0.80,0.3) (0.55,1.08)  (0.93,1.62) (0.93) (0.63) (0.65) (0.32)  (0.93,1.62) (0.93) (0.63) (0.65) (0.27)  (0.94) (0.95) (0.95) (0.95) (0.65) (0.27)  (0.94) (0.95) (0.95) (0.95) (0.95) (0.27)  (0.94) (0.95) (0.64,1.40) (0.55) (0.27)  (0.95) (0.96) (0.96) (0.96) (0.96) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.96) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.</td> <td>eats</td> <td></td>	5.2 9.1 6.5 84 5.6 9.6 45  (0.44) (0.66) (0.42) (0.88) (0.42) (0.79) (0.36)  (0.44) (0.66) (0.42) (0.88) (0.42) (0.79) (0.36)  (1.45,2.23) (1.01,1.71) (1.42,2.27) (1.05,1.23)  (1.07,1.82) (0.09,1.8) (0.07,2.128) (0.57,1.07)  (0.91,1.61) (0.60,1.8) (0.65,1.07) (0.57,1.07)  (0.92,1.62) (0.93) (0.60,1.8) (0.80,0.3) (0.55,1.08)  (0.93,1.62) (0.93) (0.63) (0.65) (0.32)  (0.93,1.62) (0.93) (0.63) (0.65) (0.27)  (0.94) (0.95) (0.95) (0.95) (0.65) (0.27)  (0.94) (0.95) (0.95) (0.95) (0.95) (0.27)  (0.94) (0.95) (0.64,1.40) (0.55) (0.27)  (0.95) (0.96) (0.96) (0.96) (0.96) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.96) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.56) (0.56) (0.56) (0.56) (0.56)  (0.96) (0.96) (0.96) (0.96) (0.56) (0.	eats													
(144) (1056) (0.42) (138) (0.42) (0.79) (0.36) (1.04) (0.39) (1.04) (0.56) (0.42) (1.027) (1.01,171) (1.42,227) (1.07,143) (1.40,124) (1.05,143) (1.07,143) (1.07,143) (1.07,143) (1.07,143) (1.07,143) (1.07,143) (1.07,143) (1.07,143) (1.07,143) (1.06,116) (1.06,1	(044)         (066)         (042)         (088)         (042)         (079)         (036)           (Model 1 <sup>b</sup> )         1.0         1.83         1.0         1.32         1.0         1.79         1.0           (Model 2 <sup>c</sup> )         1.0         1.440         1.0         0.96         1.0         0.78         1.0           (Model 3 <sup>c</sup> )         1.0         1.21         1.0         0.96         1.0         0.78         1.0           (Model 3 <sup>c</sup> )         1.0         1.21         1.0         0.84         1.0         0.67         1.0           (Model 4 <sup>c</sup> )         1.0         1.21         1.0         0.84         1.0         0.67         1.0           (Model 4 <sup>c</sup> )         1.0         1.21         1.0         0.84         1.0         0.67         1.0           (Model 1         1.0         1.20         0.89         1.0         0.65         0.65         0.32           (Model 3         1.0         1.51         1.0         1.7         0.65         0.65         0.0           (Model 4         1.0         0.28         1.0         1.17         1.0         0.83         1.0           (Model 3         1.0         0.29	5.2	9.1	6.5	8.4	5.6	9.6	4.5	14.0	6.5	12.1	6.7	18.6	0.9	10.2
I, Model I	1, Model 1 <sup>b</sup> 1,0         1,83         1,0         1,32         1,0         1,79         1,0           1, Model 2 <sup>c</sup> 1,0         1,445,232         (101,171)         (142,227)         1,0           1, Model 3 <sup>c</sup> 1,0         1,21         1,0         0.94         1,0         0.67         1,0           1, Model 4 <sup>c</sup> 1,0         1,21         1,0         0.84         1,0         0.67         1,0           1, Model 4 <sup>c</sup> 1,0         1,20         1,0         0.84         1,0         0.67         1,0           1, Model 7         1,0         1,20         1,0         0.66,1         1,0         0.67         1,0           1, Model 9         1,0         1,51         1,0         0.65         1,0         0.65         1,0           1, Model 1         1,0         1,51         1,0         1,52         1,0         1,0         1,0           1, Model 1         1,0         1,53         0,09         1,0         1,0         1,0         1,0           1, Model 2         1,0         1,17,214         1,0         0,65         1,0         1,0           1, Model 3         1,0         0,98         1,0			(0.42)	(0.88)	(0.42)	(0.79)	(0.36)	(1.04)	(0.39)	(1.80)	(0.38)	(5.10)	(0.40)	(0.99)
1,46,222   1,01,171   1,42,227   1,71,455   1,440,284   1,0   1,40   1,0   1,00   1,	(145,232)       (101,171)       (142,227)         (Model 2 <sup>e</sup> )       1.0       0.96       1.0       0.78       1.0         (Model 3 <sup>e</sup> )       1.0       1.2       0.057,128)       1.0       0.57,107)       1.0         (Model 4 <sup>e</sup> )       1.0       1.2       1.0       0.89       1.0       0.57,107)       1.0         (Model 4 <sup>e</sup> )       1.0       1.2       1.0       0.89       1.0       0.77       1.0         (Model 1)       1.0       1.2       0.0       0.0       1.0       0.77       1.0         (Model 1)       1.0       1.2       0.0       0.0       0.0       0.77       1.0         (Model 2)       1.0       0.89, 1.62       0.0       0.0       0.0       0.0       0.3       0.0		1.83	1.0	1.32	1.0	1.79	1.0	3.44	1.0	1.99	1.0	3.20	1.0	1.78
I, Model 2 <sup>c</sup> 1,0         1,0         1,0         0.06         1,0         0.78         1,0         1,28         1,0         1,28         1,0         1,0         1,0         1,0         0.04         1,0         0.07         1,0         2,64,453         1,0         1,28         1,0         1,0         1,0         1,0         0.08         1,0         0.057         1,0         2,64         1,0         1,0         1,0         1,0         0.08         1,0         0.057,13         1,0         0.08         1,0         1,0         1,0         1,0         0.08         1,0         1,2         1,0         1,0         1,0         1,0         0.09         1,0	1, Model 12*         1,0         1,40         1,0         0.96         1,0         0.78         1,0           1, Model 3**         1,0         1,21         1,0         0.84         1,0         0.657,107)         1,0           1, Model 4**         1,0         1,21         1,0         0.880         1,0         0.657,107)         1,0           1, Model 4**         1,0         1,0         0.890         1,0         0.77         1,0           1, Model 1         1,0         1,14         1,99         1,0         0.657,113         0.655,1089         1,0           1, Model 2         1,0         1,14         1,99         1,0         0.657,1209         0.361         0.655,1089         1,0           1, Model 3         1,0         1,14         1,99         1,0         1,124         1,0         0.83         1,0         0.657,1209         1,0         0.35         1,0         0.657,1209         1,0         0.657,1209         1,0         0.35         1,0         0.657,1209         1,0         0.35         1,0         0.657,1209         1,0         0.657,1209         1,0         0.657,1209         1,0         0.657,1209         1,0         0.657,1209         1,0         0.657,1209		(1.45, 2.32)		(1.01, 1.71)		(1.42, 2.27)		(2.71, 4.35)		(1.40, 2.84)		(1.63, 6.17)		(1.38, 2.29)
(107,182) (107,183) (0.27,128) (0.57,107) (246,453) (0.87,187) (0.	, Model 3 <sup>d</sup> 1.0         (1.07, 1.82)         (0.72, 1.28)         (0.57, 1.07)           , Model 4 <sup>e</sup> 1.0         1.21         1.0         0.84         1.0         0.67         1.0           , Model 4 <sup>e</sup> 1.0         1.21         1.0         0.84         1.0         0.67         1.0           , Model 4 <sup>e</sup> 1.0         1.20         1.0         0.69         1.0         0.77         1.0           , Model 1         1.0         1.51         1.0         0.657, 1.13         0.655, 1.08         1.0           , Model 1         1.0         1.51         1.0         0.657, 1.13         0.655, 1.08         0.655         0.32           , Model 2         1.0         0.63         1.0         1.64         1.0         0.659         1.0         0.659         1.0         0.657, 1.08         1.0         0.659         1.0         0.659         1.0         0.659         1.0         0.659         1.0         0.659         1.0         0.659         1.0         0.659         1.0         0.659         1.0         0.659         1.0         0.659         1.0         0.659         1.0         0.659         1.0         0.659         1.0         0.659         <		1.40	1.0	96:0	1.0	0.78	1.0	3.34	1.0	1.28	1.0	1.76	1.0	1.29
1, Model 3 <sup>4</sup> 1,0         121         1,0         0.84         1,0         0.67         1,0         2.88         1,0         123         1,0           1, Model 4°         1,0         (1,10)         0.048,0.93         1,0         2.549         1,0         1,27         1,0           1, Model 4°         1,0         1,20         1,0         0.77         1,0         0.05         1,0         1,0         1,27         1,0 <td>1, Model 3<sup>d</sup>         1.0         1.21         1.0         0.84         1.0         0.67         1.0           1, Model 4<sup>e</sup>         1.0         1.20         1.0         0.60, 1.18         0.648, 0.93         1.0           1, Model 4<sup>e</sup>         1.0         1.20         1.0         0.66, 1.18         0.057, 1.03         0.077         1.0           1, Model 1         1.0         1.21         0.057, 1.13         0.655, 1.08         0.625         0.63         0.659         0.023         0.055, 1.08         0.055         0.053         0.055         0.053         0.055         0.053         0.055         0.055         0.053         0.055         0.053         0.053         0.055         0.053</td> <td></td> <td>(1.07, 1.82)</td> <td></td> <td>(0.72, 1.28)</td> <td></td> <td>(0.57, 1.07)</td> <td></td> <td>(2.46, 4.53)</td> <td></td> <td>(0.87, 1.87)</td> <td></td> <td>(0.86, 3.59)</td> <td></td> <td>(0.96, 1.73)</td>	1, Model 3 <sup>d</sup> 1.0         1.21         1.0         0.84         1.0         0.67         1.0           1, Model 4 <sup>e</sup> 1.0         1.20         1.0         0.60, 1.18         0.648, 0.93         1.0           1, Model 4 <sup>e</sup> 1.0         1.20         1.0         0.66, 1.18         0.057, 1.03         0.077         1.0           1, Model 1         1.0         1.21         0.057, 1.13         0.655, 1.08         0.625         0.63         0.659         0.023         0.055, 1.08         0.055         0.053         0.055         0.053         0.055         0.053         0.055         0.055         0.053         0.055         0.053         0.053         0.055         0.053		(1.07, 1.82)		(0.72, 1.28)		(0.57, 1.07)		(2.46, 4.53)		(0.87, 1.87)		(0.86, 3.59)		(0.96, 1.73)
Model 4*         10         (091,161)         (060,118)         (048,093)         (205,397)         (084,178)           Model 4*         10         1,20         10         080         10         0.77         10         2,49         10         127         10           Model 1         10         1,20         10         0.657,113         (055,108)         (178,346)         (086,187)         10         127         10           Model 1         10         1.59         4.3         6.6         4.0         6.4         3.4         8.9         4.5         8.5         4.7           Model 2         1.0         1.11         10         1.52         1.0         1.64         1.0         2.77         1.0         1.96         1.0           Model 3         1.0         1.22         1.0         1.64         1.0         2.66         1.0         1.24         1.0         1.24         1.0         1.24         1.0         1.24         1.0         1.23         1.0         1.24         1.0         1.23         1.0         1.23         1.0         1.23         1.0         1.23         1.23         4.7         4.7         1.0         1.24         1.0         1.24	(, Model 4"         1.0         1.20         1.0         0.66, 118)         (0.48, 0.93)           (, Model 4"         1.0         1.20         1.0         0.80         1.0         0.77         1.0           (, Model 1"         1.20         1.0         0.83         1.0         0.655, 1.08)         1.0         0.77         1.0           (, Model 2"         1.0         1.51         1.0         1.58         1.0         0.655         (0.32)         (0.32)         (0.65)         (0.65)         (0.32)         (0.32)         (0.65)         (0.65)         (0.65)         (0.65)         (0.65)         (0.65)         (0.65)         (0.65)         (0.65)         (0.65)         (0.65)         (0.65)         (0.65)         (0.75)		1.21	1.0	0.84	1.0	0.67	1.0	2.85	1.0	1.23	1.0	1.86	1.0	1.16
b, Model 4*         1,0         1,20         1,0         0,77         1,0         2,49         1,0         1,27         1,0           b, Model 4*         1,0         1,20         1,0         0,77         1,0         1,73,346         1,0         1,27         1,0           4,0         5.9         4,3         6.6         4,0         6,4         3,4         8,9         4,5         8,5         4,7           (0.39)         (0.54)         (0.35)         (0.79)         (0.36)         (0.65)         (0.32)         (0.86)         (0.33)         (1.33)         (0.32)         (0.86)         (0.33)         (1.33)         (0.32)         (0.86)         (0.33)         (0.70)         (0.65)         (0.65)         (0.82)         (0.86)         (0.33)         (0.30)         (0.65)         (0.65)         (0.65)         (0.27)         (0.27)         (0.27)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)         (0.86)         (0.70)         (0.70)         (0.87)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)         (0.70)	Wodel 4*         1.0         1.20         1.0         0.80         1.0         0.77         1.0           Wodel 4*         1.0         (0.89, 162)         (0.57, 1.13)         (0.55, 1.08)         1.0           (0.39)         (0.54)         (0.35)         (0.54)         (0.35)         (0.55, 1.08)         (0.32)           Wodel 1         1.0         1.51         1.0         1.58         1.0         6.64         3.4           Wodel 2         1.0         1.51         1.0         1.58         1.0         6.65         (0.32)           Wodel 3         1.0         0.98         1.0         1.17, 2.14)         1.0         0.83         1.0           Wodel 4         1.0         0.98         1.0         0.65, 1.20)         1.0         0.74         1.0           Wodel 4         1.0         0.98         1.0         0.64, 1.40)         1.0         0.57, 1.02)         1.0           Wodel 5         1.0         0.29         1.0         0.64, 1.40)         0.65, 1.10)         1.0           Wodel 7         1.0         0.29         1.0         0.64, 1.40)         0.65, 1.10)         1.0           Wodel 8         1.0         1.64         1.0		(0.91, 1.61)		(0.60, 1.18)		(0.48, 0.93)		(2.05, 3.97)		(0.84, 1.78)		(0.92, 3.76)		(0.85, 1.58)
40         5.9         4.3         4.8         4.5         4.5         4.7	40       5.9       4.3       6.6       4.0       6.4       3.4         (0.39)       (0.54)       (0.35)       (0.35)       (0.79)       (0.36)       (0.65)       (0.32)         (0.39)       (0.54)       (0.35)       (0.79)       (0.36)       (0.65)       (0.32)         (0.39)       (0.54)       (0.35)       (0.79)       (0.36)       (0.65)       (0.32)         (0.44)       (0.11)       1.0       (0.11)       1.0       0.83       1.0         (0.71,136)       (0.87,171)       1.0       0.657,120)       1.0         (0.71,136)       (0.69,148)       1.0       0.657,120)       1.0         (0.70,138)       1.0       (0.64,140)       (0.67,110)       1.0         (0.70,138)       1.0       (0.64,140)       (0.50,110)       1.0         (0.70,138)       1.0       (0.64,140)       (0.50,110)       1.0         (0.70,138)       1.0       (0.64,140)       (0.50,110)       1.0         (0.70,138)       1.0       (0.64,140)       (0.50,110)       1.0         (0.70,138)       1.0       (0.64,140)       (0.50,110)       1.0         (0.70,138)       1.0       (0.64,140)       (0.50,110)		1.20	1.0	0.80	1.0	0.77	1.0	2.49	1.0	1.27	1.0	1.74	1.0	1.23
4.0         5.9         4.3         6.6         4.0         6.4         3.4         8.9         4.5         8.5         4.7           (0.39)         (0.54)         (0.35)         (0.79)         (0.36)         (0.65)         (0.32)         (0.86)         (0.33)         (1.53)         (0.32)           Wodel 1         1.0         1.58         1.0         1.64         1.0         2.77         1.0         1.96         1.0           Wodel 2         1.0         1.51         1.0         1.28         1.0         1.64         1.0         2.77         1.0         1.96         1.0           Wodel 3         1.0         1.58         1.0         1.01         1.0         1.22         1.0         1.24         1.0         1.24         1.0           Wodel 3         1.0         0.08         1.0         1.01         1.0         0.74         1.0         2.27         1.0         1.15         1.0           Wodel 4         1.0         0.09         0.05         1.0         0.74         1.0         0.227         1.0         1.15         1.0           Wodel 4         1.0         0.09         0.069         1.0         0.274         1.0         <	4.0         5.9         4.3         6.6         4.0         6.4         3.4           (0.39)         (0.54)         (0.35)         (0.79)         (0.36)         (0.65)         (0.32)           (0.39)         (0.54)         (0.35)         (0.79)         (0.36)         (0.65)         (0.32)           (0.39)         (0.54)         (0.35)         (0.79)         (0.36)         (0.65)         (0.32)           (0.41, 1.59)         (1.17, 2.14)         (1.17, 2.17)         (0.87, 1.12)         (0.83)         1.0           (0.81, 1.50)         (0.81, 1.50)         (0.87, 1.71)         (0.57, 1.20)         (0.69)         1.0           (0.71, 1.36)         (0.71, 1.36)         (0.69, 1.48)         (0.47, 1.02)         1.0         0.74         1.0           (0.70, 1.38)         (0.70, 1.38)         (0.66, 1.40)         (0.55)         (0.57, 1.10)         1.0         0.74         1.0           (0.32)         (0.46)         (0.29)         (0.64, 1.40)         (0.55)         (0.27)         (0.57)         (0.57)         (0.57)           (0.32)         (0.46)         (0.29)         (0.65)         (0.30)         (0.55)         (0.27)           (0.32)         (0.46)         (0.29) <t< td=""><td></td><td>(0.89, 1.62)</td><td></td><td>(0.57, 1.13)</td><td></td><td>(0.55, 1.08)</td><td></td><td>(1.78, 3.46)</td><td></td><td>(0.86, 1.87)</td><td></td><td>(0.86, 3.54)</td><td></td><td>(0.90, 1.69)</td></t<>		(0.89, 1.62)		(0.57, 1.13)		(0.55, 1.08)		(1.78, 3.46)		(0.86, 1.87)		(0.86, 3.54)		(0.90, 1.69)
4.0 5.9 4.3 6.6 4.0 6.4 3.4 8.9 4.5 8.5 4.7 (3.2) (3.3	4.0 5.9 4.3 6.6 4.0 6.4 3.4 (0.39) (0.39) (0.54) (0.35) (0.79) (0.36) (0.65) (0.32) (0.32) (0.54) (0.35) (0.79) (0.36) (0.65) (0.32) (0.32) (0.35) (0.79) (0.36) (0.65) (0.32) (0.32) (0.37) (0.37, 1.24) (0.38, 1.0 1.14) (0.38, 1.15) (0.38, 1.15) (0.38, 1.14) (0.38, 1.14) (0.38, 1.14) (0.38, 1.14) (0.39, 1.48) (0.39, 1.48) (0.39, 1.10) (0.31, 1.34) (0.39, 1.48) (0.39, 1.48) (0.39, 1.14) (0.39,	h Pain													
% Cl, Model I         1,0         1,54         (0.54)         (0.54)         (0.54)         (0.54)         (0.65)         (0.65)         (0.86)         (0.33)         (153)         (0.32)           % Cl, Model I         1,51         1,0         1,58         1,0         1,64         1,0         2,77         1,0         1,96         1,0           % Cl, Model 2         1,0         1,11         1,0         1,22         1,0         2,66         1,0         1,24         1,0           % Cl, Model 3         1,0         0.08         1,0         1,01         1,0         0.69         1,0         2,27         1,0         1,15         1,0           % Cl, Model 4         1,0         0.98         1,0         1,01         1,0         0.69         1,0         2,27         1,0         1,15         1,0           % Cl, Model 4         1,0         0.98         1,0         0.94         1,0         0.74         1,0         2,27         1,0         1,15         1,0         1,15         1,0         1,15         1,0         1,15         1,0         1,15         1,0         1,15         1,0         1,15         1,0         1,15         1,0         1,15         1,0	% CI), Model 1       1,0       1,51       1,0       1,58       1,0       1,64       1,0         % CI), Model 2       1,0       1,51       1,0       1,58       1,0       1,64       1,0         % CI), Model 2       1,0       1,11       1,0       1,122       1,0       0,83       1,0         % CI), Model 3       1,0       0,98       1,0       1,01       1,0       0,69       1,0         % CI), Model 4       1,0       0,98       1,0       0,095       1,0       0,74       1,0         % CI), Model 4       1,0       0,98       1,0       0,064, 1,40)       0,650, 1,10)       1,0       1,0         % CI), Model 5       1,0       0,29       1,0       1,43       1,0       1,69       1,0         % CI), Model 6       1,0       1,43       1,0       1,43       1,0       1,69       1,0         % CI), Model 7       1,0       1,24       1,0       0,99, 2,06       0,30       0,55, 1,31       1,0         % CI), Model 8       1,0       1,24       1,0       0,99, 2,06       1,0       0,66, 1,10       0,86       1,0         % CI), Model 9       1,0       1,24       1,0       0,98	4.0	5.9	4.3	9.9	4.0	6.4	3.4	8.9	4.5	8.5	4.7	11.9	4.1	9.7
% CJ, Model 1 1.0 1.51 1.0 1.58 1.0 1.64 1.0 2.77 1.0 1.96 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0	% CI), Model 1 1.0 1.51 1.0 1.58 1.0 1.64 1.0 1.0   (1.14, 1.99)	(0.39		(0.35)	(0.79)	(0.36)	(0.65)	(0.32)	(0.86)	(0.33)	(1.53)	(0.32)	(4.21)	(0.34)	(0.86)
% Cl, Model 2         1.0         1.14, 1.99 (1.17, 2.14)         (1.24, 2.17)         (209,366)         (1.30, 2.97)           % Cl, Model 2         1.0         1.11         1.0         1.22         1.0         0.83         1.0         2.66         1.0         1.24         1.0           % Cl, Model 3         1.0         0.83         1.0         0.69         1.0         2.66         1.0         1.24         1.0           % Cl, Model 4         1.0         0.98         1.0         0.055         1.0         0.74         1.0         2.00         1.0         1.15         1.0           % Cl, Model 4         1.0         0.98         1.0         0.055         1.0         0.74         1.0         2.00         1.0         1.15         1.0           % Cl, Model 5         1.0         0.29         1.0         0.74         1.0         2.70         1.0         1.25         1.0           % Cl, Model 1         1.0         1.69         1.0         0.74         1.0         2.74         6.1         3.2         4.5         3.2           % Cl, Model 2         1.0         1.43         1.0         1.69         1.0         2.74         6.1         3.2         4.5	% CI), Model 2 1.0 1.11 1.0 1.22 1.0 0.83 1.0 (881, 1.50) (881, 1.50) (887, 1.71) (687, 1.71) (687, 1.20) (881, 1.50) (881, 1.50) (887, 1.71) (687, 1.20) (881, 1.50) (881, 1.			1.0	1.58	1.0	1.64	1.0	2.77	1.0	1.96	1.0	2.70	1.0	1.92
% Cl), Model 2         1.0         1.11         1.0         1.22         1.0         0.83         1.0         2.66         1.0         1.24         1.0           % Cl), Model 3         1.0         0.69         1.0         0.69         1.0         2.27         1.0         1.15         1.0           % Cl), Model 4         1.0         0.98         1.0         1.01         1.0         0.69         1.0         2.27         1.0         1.15         1.0           % Cl), Model 4         1.0         0.98         1.0         0.95         1.0         0.74         1.0         2.00         1.0         1.25         1.0           % Cl), Model 9         1.0         0.995         1.0         0.74         1.0         2.00         1.0         1.25         1.0           % Cl), Model 1         1.0         0.695         1.0         0.74         1.0         2.00         1.0         1.25         1.0           % Cl), Model 1         1.0         1.69         1.0         0.25         0.27         0.72         0.28         1.15         1.0           % Cl), Model 2         1.0         1.33         1.0         1.43         1.0         1.24         1.0	% CI), Model 2       1.0       1.11       1.0       1.22       1.0       0.83       1.0         % CI), Model 3       1.0       0.98       1.0       1.01       1.0       0.69       1.0         % CI), Model 4       1.0       0.98       1.0       1.01       0.09       1.0         % CI), Model 4       1.0       0.98       1.0       0.95       1.0       0.74       1.0         % CI), Model 1       1.0       0.98       1.0       0.64, 1.40)       0.74       1.0         % CI), Model 2       1.0       1.69       1.0       1.43       1.0       0.55)       0.27)         % CI), Model 3       1.0       1.24       1.0       0.99, 2.06)       1.0       0.74       1.0         % CI), Model 3       1.0       1.24       1.0       0.74       1.0       0.86       1.0         % CI), Model 4       1.0       1.24       1.0       0.74       1.0       0.86       1.0         % CI), Model 4       1.0       1.26       1.0       0.74       1.0       0.89       1.0         % CI), Model 4       1.0       1.26       1.0       0.87       1.0       0.89       1.0         %		(1.14, 1.99)		(1.17, 2.14)		(1.24, 2.17)		(2.09, 3.66)		(1.30, 2.97)		(1.22, 6.06)		(1.43, 2.58)
% Cl), Model 3	% CI), Model 3		1.11	1.0	1.22	1.0	0.83	1.0	2.66	1.0	1.24	1.0	1.45	1.0	1.45
% Cl), Model 3 1.0 0.98 1.0 1.01 1.0 0.69 1.0 2.27 1.0 1.15 1.0 1.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0	% CJ), Model 3 1.0 0.98 1.0 1.01 1.0 0.69 1.0  % CJ), Model 4 1.0 0.98 1.0 0.95 1.0 0.47, 1.02)  % CJ), Model 4 1.0 0.98 1.0 0.95 1.0 0.74 1.0  2.6 4.3 3.0 4.3 2.7 4.5 2.4  % CJ), Model 1 1.0 1.69 1.0 1.43 1.0 1.65 1.0  % CJ), Model 2 1.0 1.24 1.0 0.98 1.0 0.56, 1.31)  % CJ), Model 4 1.0 1.26 1.0 0.87 1.0 0.89 1.0  % CJ), Model 5 1.0 1.26 1.0 0.87 1.0 0.89 1.0  % CJ), Model 6 1.0 1.26 1.0 0.87 1.0 0.89 1.0  % CJ), Model 7 1.0 0.84, 1.85 0.88 1.0 0.89 1.0 0.89 1.0  % CJ), Model 8 1.0 0.84, 1.81 0.88 1.0 0.89 1.0		(0.81, 1.50)		(0.87, 1.71)		(0.57, 1.20)		(1.87, 3.80)		(0.78, 1.96)		(0.61, 3.44)		(1.03, 2.02)
% CJ), Model 4 1.0 0.98 1.0 0.69, 148) (0.77, 1.02) (1.53, 3.37) (0.72, 1.82) (0.70, 1.38) (0.64, 1.40) (0.50, 1.10) (1.35, 2.95) (0.70, 1.38) (0.64, 1.40) (0.50, 1.10) (1.35, 2.95) (0.78, 2.02) (0.78, 2.02) (0.70, 1.38) (0.65) (0.29) (0.65) (0.29) (0.55) (0.27) (0.72) (0.72) (0.28) (1.15) (0.27) (0.28) (0.27) (0.28) (0.27) (0.28) (0.27) (0.28) (0.27) (0.28) (0.27) (0.28) (0.27) (0.27) (0.28) (0.27) (0.27) (0.28) (0.27) (0.27) (0.28) (0.27) (0.27) (0.28) (0.27) (0.27) (0.28) (0.27) (0.27) (0.27) (0.28) (0.27) (0.27) (0.28) (0.27) (0.27) (0.28) (0.27) (0.27) (0.27) (0.28) (0.27) (0.27) (0.27) (0.28) (0.27) (0.27) (0.27) (0.28) (0.27) (0.27) (0.28) (0.27	% CI), Model 4 1.0 0.98 1.0 0.69, 148) (0.47, 1.02)  2.6 4.3 3.0 4.3 2.7 4.5 1.0  (0.32) (0.46) (0.29) (0.65) (0.30) (0.55) (0.27)  % CI), Model 1 1.0 1.69 1.0 1.43 1.0 1.69 1.0  (1.21, 2.36) (0.99, 2.06) (0.55) (0.27)  % CI), Model 2 1.0 1.24 1.0 0.98 1.0 0.74 1.0  (0.95, 1.88) (0.78, 1.65) (0.56, 1.31)  % CI), Model 4 1.0 1.26 1.0 0.87 1.0 0.89 1.0  (0.84, 1.81) (0.55, 1.39) (0.55, 1.42)  4.9 7.0 5.6 6.7 4.8 8.1 3.7  (0.43) (0.58) (0.39) (0.80) (0.89) (0.73) (0.33)	Э	0.98	1.0	1.01	1.0	69.0	1.0	2.27	1.0	1.15	1.0	1.48	1.0	1.27
% CI), Model 4 1.0 0.98 1.0 0.95 1.0 0.74 1.0 2.00 1.0 125 1.0 1.0 (0.70, 1.38) (0.64, 1.40) (0.50, 1.10) (1.35, 2.95) (0.73, 2.02) (0.73, 2.23) (0.73, 2.23) (0.	% CI), Model 4 1.0 0.98 1.0 0.95 1.0 0.74 1.0 (0.50, Model 4 1.0 (0.70, 1.38) (0.64, 1.40) (0.50, 1.10) (0.50, 1.10) (0.32) (0.46) (0.29) (0.65) (0.30) (0.55) (0.27) (0.27) (0.99, 2.06) (1.21, 2.36) (0.99, 2.06) (1.21, 2.36) (0.95, 1.88) (0.78, 1.65) (0.56, 1.31) (0.95, 1.88) (0.78, 1.65) (0.56, 1.31) (0.84, 1.85) (0.84, 1.81) (0.63, 1.53) (0.56, 1.42) (0.64, 1.17) (0.84, 1.91) (0.55, 1.39) (0.59, 0.89) (0.78, 1.63) (0.56, 1.42) (0.56, 1.42) (0.56, 1.42) (0.56, 1.42) (0.56, 1.39) (0.59, 0.89) (0.78) (0.78, 1.39) (0.78, 1.39) (0.78, 1.39) (0.78, 1.39) (0.78) (0.78) (0.78) (0.78) (0.78) (0.78)		(0.71, 1.36)		(0.69, 1.48)		(0.47, 1.02)		(1.53, 3.37)		(0.72, 1.82)		(0.63, 3.46)		(0.90, 1.79)
2.6 4.3 3.0 4.3 2.7 4.5 2.4 6.1 3.2 4.5 3.2 (0.78, 2.02)  2.6 4.3 3.0 4.3 2.7 4.5 2.4 6.1 3.2 4.5 3.2 (0.27) (0.28) (1.15) (0.27) (0.27) (0.28) (1.15) (0.27	2.6 4.3 3.0 4.3 2.7 4.5 2.4 (0.32) (0.65) (0.30) (0.55) (0.27) (0.32) (0.46) (0.29) (0.65) (0.30) (0.55) (0.27) (0.27) (0.29, 2.06) (0.30) (0.55) (0.27) (0.27) (0.29, 2.06) (0.30) (0.55) (0.27) (0.27, 2.36) (0.95, 1.88) (0.78, 1.65) (0.78, 1.65) (0.56, 1.31) (0.95, 1.88) (0.78, 1.65) (0.78, 1.65) (0.56, 1.31) (0.84, 1.85) (0.84, 1.81) (0.63, 1.53) (0.46, 1.17) (0.84, 1.81) (0.84, 1.91) (0.55, 1.39) (0.55, 1.42) (0.55, 1.42) (0.55, 1.42) (0.55, 1.42) (0.55, 1.39) (0.56, 1.42) (0.55, 1.39) (0.59) (0.78) (0.78) (0.33)		0.98	1.0	0.95	1.0	0.74	1.0	2.00	1.0	1.25	1.0	1.48	1.0	1.35
2.6 4.3 3.0 4.3 2.7 4.5 2.4 6.1 3.2 4.5 3.2 3.2 (2.77) (0.72) (0.28) (1.15) (0.27) (0.	2.6 4.3 3.0 4.3 2.7 4.5 2.4 (0.32) (0.65) (0.30) (0.55) (0.27) (0.27) (0.32) (0.46) (0.29) (0.65) (0.30) (0.55) (0.27) (0.27) (0.29, 2.06) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.24, 1.33) (1.24, 1.44) (1.0, 1.1		(0.70, 1.38)		(0.64, 1.40)		(0.50, 1.10)		(1.35, 2.95)		(0.78, 2.02)		(0.61, 3.58)		(0.94, 1.93)
2.6 4.3 3.0 4.3 2.7 4.5 2.4 6.1 3.2 4.5 3.2 (3.20) (0.55) (0.20) (0.55) (0.27) (0.22) (0.28) (1.15) (0.27) (0.27) (0.28) (1.15) (0.27) (0.27) (0.28) (1.15) (0.27) (0.27) (0.28) (1.15) (0.27) (0.27) (0.28) (1.15) (0.27) (0.27) (0.28) (0.27) (0.27) (0.28) (0.27) (0.27) (0.28) (0.27) (0.28) (0.27) (0.28) (0.27) (0.28) (0.27) (0.28) (0.27) (0.28) (0.27) (0.28) (0.27) (0.28) (0.27) (0.27) (0.28) (0.27) (0.27) (0.27) (0.28) (0.27) (0.27) (0.27) (0.27) (0.27) (0.27) (0.27) (0.27) (0.27) (0.27) (0.29, 2.6) (0.29, 2.06) (0.29, 2	2.6 4.3 3.0 4.3 2.7 4.5 2.4 (0.32) (0.32) (0.46) (0.29) (0.65) (0.30) (0.55) (0.27) (0	SS													
(9.32)       (0.46)       (0.29)       (0.65)       (0.30)       (0.55)       (0.27)       (0.72)       (0.28)       (1.15)       (0.27)         5% Cl), Model 1       1.0       1.69       1.0       1.69       1.0       1.69       1.0       1.43       1.0       1.69       1.0       1.70       1.43       1.0       1.69       1.0       1.0       1.43       1.0       1.69       1.0       1.0       1.43       1.0       1.43       1.0       1.43       1.0       1.43       1.0       1.43       1.0       1.43       1.0       1.63       1.0       1.0       1.43       1.0       1.0       1.43       1.0       1.0       1.0       1.0       1.0       1.0       1.0       1.0       1.0       1.0       0.56       1.1       1.0       0.53       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.55       1.0       0.53       0.0       0.33	(0.32) (0.46) (0.29) (0.65) (0.30) (0.55) (0.27) (0.27) (0.27) (0.27) (0.27) (0.29) (0.65) (0.30) (0.55) (0.27) (0.27) (0.29, 2.06) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.21, 2.36) (1.25, 1.38) (1.26, 1.14) (1.26, 1.15) (1.26, 1.37) (1.26, 1.27) (1.	2.6		3.0	4.3	2.7	4.5	2.4	6.1	3.2	4.5	3.2	11.9	3.0	4.6
5% Cl), Model 1 1.0 1.69 1.0 1.43 1.0 1.69 1.0 2.70 1.0 1.43 1.0 1.0 5% Cl), Model 2 1.0 1.33 1.0 1.14 1.0 0.86 1.0 2.54 1.0 0.92 1.0 1.0 1.34 1.0 0.95, 1.69 1.0 0.55, 1.38 1.0 1.14 1.0 0.86 1.0 2.54 1.0 0.92 1.0 0.95, 1.88 1.0 1.24 1.0 0.98 1.0 0.74 1.0 2.25 1.0 0.87 1.0 0.84 1.0 0.84, 1.85 1.0 0.87 1.0 0.89 1.0 2.05 1.0 0.84 1.0 0.84 1.0 0.87 1.0 0.89 1.0 2.05 1.0 0.84 1.0 0.84 1.0 0.85, 1.39 (0.55, 1.39) (0.55, 1.39) (0.55, 1.42) (0.55, 1.39) (0.56, 1.42) (0.55, 1.42) (0.55, 1.39) (0.59) (0.73) (0.39) (0.39) (0.73) (0.33) (0.39) (0.35) (0.39) (0.73) (0.33) (0.38) (0.35) (0.35) (0.35)	5% CJ, Model 1 1.0 1.69 1.0 1.43 1.0 1.69 1.0 1.0 5% CJ, Model 2 1.0 1.33 1.0 1.14 1.0 0.86 1.0 1.24, 2.36) 1.0 1.14 1.0 0.86 1.0 1.24 1.0 0.78, 1.65 1.0 0.74 1.0 0.84, 1.85 1.0 0.63, 1.53 1.0 1.26 1.0 0.87 1.0 0.89 1.0 0.89 1.0 0.84, 1.91 1.0 0.87 1.0 0.89 1.0 0.89 1.0 0.89 1.0 0.84, 1.91 1.0 0.87 1.0 0.89 1.0 0.89 1.0 0.89, 1.0 0.89, 1.0 0.89, 1.0 0.89, 1.0 0.89, 1.0 0.89, 1.0 0.89, 1.0 0.89, 1.0 0.89, 1.0 0.89, 0.89 1.0 0.89, 0.89 1.0 0.89, 0.89 0.89 1.0 0.89 0.89 0.89 0.89 0.89 0.89 0.89 0.	(0.32		(0.29)	(0.65)	(0:30)	(0.55)	(0.27)	(0.72)	(0.28)	(1.15)	(0.27)	(4.21)	(0.29)	(0.68)
5% Cl), Model 2       1.0       1.33       1.0       1.14       1.0       0.86       1.0       2.54       1.0       0.92       1.0         5% Cl), Model 3       1.0       1.14       1.0       0.86       1.0       2.54       1.0       0.92       1.0         5% Cl), Model 3       1.0       1.24       1.0       0.78, 1.65)       (0.56, 1.31)       (1.70, 380)       (0.53, 1.58)       1.0         5% Cl), Model 4       1.0       1.24       1.0       0.98       1.0       0.74       1.0       2.25       1.0       0.87       1.0         5% Cl), Model 4       1.0       1.26       1.0       0.87       1.0       0.89       1.0       2.05       1.0       0.84       1.0         5% Cl), Model 4       1.0       1.26       1.0       0.87       1.0       0.89       1.0       2.05       1.0       0.84       1.0         6.84, 1.91)       (0.55, 1.39)       (0.56, 1.42)       (1.29, 3.27)       (0.48, 1.48)       1.0         6.49       7.0       5.6       6.7       4.8       8.1       3.7       12.1       5.       10.0       5.8         6.43       (0.58)       (0.58)       (0.73)       (0.3	5% Cl), Model 2       1.0       1.33       1.0       1.14       1.0       0.86       1.0         5% Cl), Model 3       1.0       1.14       1.0       0.86       1.0         5% Cl), Model 4       1.0       1.24       1.0       0.78       1.0       0.74       1.0         5% Cl), Model 4       1.0       1.26       1.0       0.63, 1.53       0.046, 1.17)       0.89       1.0         6% Cl), Model 4       1.0       1.26       1.0       0.87       1.0       0.89       1.0         1       4.9       7.0       5.6       6.7       4.8       8.1       3.7         1       4.9       7.0       5.6       6.7       4.8       8.1       3.7         1       0.43       0.58)       0.39)       (0.80)       (0.73)       (0.33)			1.0	1.43	1.0	1.69	1.0	2.70	1.0	1.43	1.0	4.10	1.0	1.60
5% Cl), Model 2 1.0 1.33 1.0 1.14 1.0 0.86 1.0 2.54 1.0 0.92 1.0 (0.95, 1.88) (0.78, 1.65) (0.56, 1.31) (1.70, 3.80) (0.53, 1.58) (0.55, 1.13) (0.54, 1.85) (0.54, 1.85) (0.63, 1.53) (0.63, 1.53) (0.46, 1.17) (1.42, 3.55) (0.50, 1.49) (0.84, 1.81) (0.84, 1.91) (0.55, 1.39) (0.56, 1.42) (0.56, 1.42) (0.56, 1.42) (0.56, 1.43) (0.56, 1.42) (0.56, 1.43) (0.56, 1.43) (0.56, 1.42) (0.56, 1.43) (0.56, 1.43) (0.56, 1.42) (0.56, 1.42) (0.56, 1.43) (0.56, 1.43) (0.56, 1.43) (0.56, 1.44) (0.56	5% CI), Model 2 1.0 1.33 1.0 1.14 1.0 0.86 1.0 (0.95, 1.88) (0.78, 1.65) (0.56, 1.31) (0.55, 1.88) (0.78, 1.65) (0.56, 1.31) (0.84, 1.85) (0.63, 1.53) (0.64, 1.17) (0.84, 1.91) (0.55, 1.39) (0.55, 1.42) (0.56, 1.42) (0.56, 1.42) (0.56, 1.87) (0.84, 1.91) (0.55, 1.89) (0.89) (0.73) (0.33)		(1.21, 2.36)		(0.99, 2.06)		(1.21, 2.36)		(1.94, 3.76)		(0.83, 2.48)		(1.82, 9.13)		(1.09, 2.25)
(0.95, 1.88) (0.76, 1.65) (0.56, 1.31) (1.70, 3.80) (0.53, 1.58) (0.59, 1.88) (0.56, 1.31) (1.70, 3.80) (0.53, 1.58) (0.87, 1.24) (0.63, 1.53) (0.46, 1.17) (1.42, 3.55) (0.50, 1.49) (0.84, 1.91) (0.56, 1.39) (0.56, 1.42) (0.56, 1.42) (0.56, 1.42) (0.56, 1.42) (0.56, 1.39) (0.56, 1.42) (0.56, 1.32) (0.58) (0.58) (0.89) (0.73) (0.33) (0.98) (0.36) (1.65) (0.36)	6.95, 1.88) (0.78, 1.65) (0.56, 1.31)  5% Cl), Model 3 1.0 1.24 1.0 0.98 1.0 0.74 1.0  (0.84, 1.85) (0.63, 1.53) (0.46, 1.17)  (0.84, 1.91) (0.55, 1.39) (0.56, 1.42)  (0.49) 7.0 5.6 6.7 4.8 8.1 3.7  (0.43) (0.58) (0.39) (0.80) (0.89) (0.73) (0.33)		1.33	1.0	1.14	1.0	98.0	1.0	2.54	1.0	0.92	1.0	2.59	1.0	1.16
5% Cl), Model 3 1.0 1.24 1.0 0.98 1.0 0.74 1.0 2.25 1.0 0.87 1.0 1.0 (0.84, 1.85) (0.63, 1.53) (0.46, 1.17) (1.42, 3.55) (0.50, 1.49) (0.84, 1.91) (0.55, 1.39) (0.56, 1.42) (0.56, 1.42) (1.29, 3.27) (0.48, 1.48) (0.43) (0.58) (0.39) (0.80) (0.89) (0.73) (0.33) (0.98) (0.36) (1.65) (0.36)	5% Cl), Model 3 1.0 1.24 1.0 0.98 1.0 0.74 1.0 (0.84, 1.85) (0.63, 1.53) (0.46, 1.17) (0.84, 1.91) (0.55, 1.39) (0.55, 1.42) (0.56, 1.42) (0.43) (0.58) (0.59) (0.80) (0.89) (0.73) (0.33)		(0.95, 1.88)		(0.78, 1.65)		(0.56, 1.31)		(1.70, 3.80)		(0.53, 1.58)		(1.10, 6.14)		(0.76, 1.76)
(0.84, 1.85) (0.63, 1.53) (0.46, 1.17) (142, 3.55) (0.50, 1.49) 5% Cl), Model 4 1.0 1.26 1.0 0.87 1.0 0.89 1.0 2.05 1.0 0.84 1.0 (0.84, 1.91) (0.55, 1.39) (0.56, 1.42) (1.29, 3.27) (0.48, 1.48) (0.43) (0.58) (0.39) (0.80) (0.89) (0.73) (0.33) (0.98) (0.36) (1.65) (0.36)	6.84, 1.85) (0.63, 1.53) (0.46, 1.17) 5% Cl), Model 4 1.0 1.26 1.0 0.87 1.0 0.89 1.0 (0.84, 1.91) (0.55, 1.39) (0.56, 1.42) 4.9 7.0 5.6 6.7 4.8 8.1 3.7 (0.43) (0.58) (0.59) (0.80) (0.89) (0.73) (0.33)			1.0	0.98	1.0	0.74	1.0	2.25	1.0	0.87	1.0	2.60	1.0	1.05
5% Cl), Model 4 1.0 1.26 1.0 0.87 1.0 0.89 1.0 2.05 1.0 0.84 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0	5% Cl), Model 4 1.0 1.26 1.0 0.87 1.0 0.89 1.0 (0.84, 1.91) (0.55, 1.39) (0.56, 1.42) (0.56, 1.42) (0.43) (0.58) (0.59) (0.89) (0.89) (0.73) (0.33)		(0.84, 1.85)		(0.63, 1.53)		(0.46, 1.17)		(1.42, 3.55)		(0.50, 1.49)		(1.09, 6.21)		(0.67, 1.65)
(0.84, 1.91) (0.55, 1.39) (0.56, 1.42) (1.29, 3.27) (0.48, 1.48) (0.84) (0.84) (0.89) (0.73) (0.33) (0.98) (0.36) (0.36) (0.36)	(0.84, 1.91)     (0.55, 1.39)     (0.56, 1.42)       4.9     7.0     5.6     6.7     4.8     8.1     3.7       (0.43)     (0.58)     (0.39)     (0.80)     (0.89)     (0.73)     (0.33)		1.26	1.0	0.87	1.0	0.89	1.0	2.05	1.0	0.84	1.0	2.74	1.0	1.11
4.9 7.0 5.6 6.7 4.8 8.1 3.7 12.1 5.5 10.0 5.8 (0.43) (0.58) (0.39) (0.80) (0.89) (0.73) (0.33) (0.98) (0.36) (1.65) (0.36)	4.9 7.0 5.6 6.7 4.8 8.1 3.7 (0.43) (0.58) (0.39) (0.39) (0.80) (0.83)		(0.84, 1.91)		(0.55, 1.39)		(0.56, 1.42)		(1.29, 3.27)		(0.48, 1.48)		(1.13, 6.60)		(0.69, 1.76)
4.9 7.0 5.6 6.7 4.8 8.1 3.7 12.1 5.5 10.0 5.8 (0.43) (0.58) (0.39) (0.89) (0.73) (0.33) (0.98) (0.36) (1.65) (0.36)	4.9     7.0     5.6     6.7     4.8     8.1     3.7       (0.43)     (0.58)     (0.39)     (0.80)     (0.89)     (0.73)     (0.33)														
(0.58) (0.39) (0.80) (0.89) (0.73) (0.33) (0.98) (0.36) (1.65) (0.36)	(0.58) (0.39) (0.80) (0.89) (0.73) (0.33)			2.6	6.7	4.8	8.1	3.7	12.1	5.5	10.0	5.8	8.5	5.5	7.2
		(0.43		(0.39)	(0.80)	(0.89)	(0.73)	(0.33)	(0.98)	(0.36)	(1.65)	(0.36)	(3.63)	(0.39)	(0.84)

Table 5. (Continued)														
						Supplement Class	t Class							
Side-effects	Mult (OR,	Multivitamin (OR, 95% CI) <sup>a</sup>	Individual Vitamin Mineral (OR, 95%	Individual Vitamin or Mineral (OR, 95% CI)	Prc Supple (OR, 9	Protein Supplements (OR, 95% CI)	Comt Pro (OR, !	Combination Products (OR, 95% CI)	He (OR,	Herbals (OR, 95% CI)	Purport Ana (OR,	Purported Steroid Analogues (OR, 95% CI)	O (OR,	Other (OR, 95% CI)
OR (95% CI), Model 1	1.0	1.45	1.0	1.22 (0.91, 1.63)	1.0	1.75 (1.36, 2.26)	1.0	3.55 (2.75, 4.58)	1.0	1.91	1.0	1.50	1.0	1.35
OR (95% CI), Model 2	1.0	1.11 (0.83, 1.47)	1.0	1.01	1.0	0.83	1.0	3.73 (2.68, 5.17)	1.0	1.43	1.0	0.85	1.0	0.99
OR (95% CI), Model 3	1.0	0.98 (0.73, 1.32)	1.0	0.93	1.0	0.73	1.0	3.25 (2.27, 4.65)	1.0	1.39 (0.93, 2.09)	1.0	0.92	1.0	0.93
OR (95% CI), Model 4	1.0	0.95 (0.70, 1.29)	1.0	0.87	1.0	0.88 (0.61, 1.25)	1.0	2.88 (2.01, 4.14)	1.0	1.47 (0.97, 2.23)	1.0	0.83	1.0	0.94 (0.66, 1.33)
Numbness/ Tingling %	2.2	3.6	2.7	3.1	1.2	6.1	4.1	6.9	2.7	4.5	2.7	8.5	2.3	4.8 (0.70)
(SE) OR (95% CI) Model 1	(0.29)	(0.43)	(0.28)	(0.55)	(0.20)	(0.64)	(0.21)	(0.76)	(0.25)	(1.15)	(0.25)	(3.63)	(0.25)	220
On (95% CI), Model 1	2 5	(1.17, 2.41)	5 6	(0.74, 1.72)	5 6	(3.51, 7.67)	<u>;</u> ;	(3.52, 7.38)	<u>;</u> ;	(1.01, 3.04)	<u> </u>	(1.30, 8.45)	<u>.</u> .	(1.50, 3.17)
	2	(0.59, 1.34)	<u> </u>	(0.47, 1.19)	2	(1.84, 4.87)	2	(1.81, 4.38)	2	(1.01, 3.04)	2	(0.52, 3.23)	2	(1.01, 2.39)
OR (95% CI), Model 3	1.0	0.80 (0.51, 1.25)	1.0	0.63 (0.38, 1.05)	1.0	2.50 (1.40, 4.44)	1.0	2.32 (1.45, 3.71)	1.0	0.82 (0.46, 1.47)	1.0	1.26 (0.50, 3.16)	1.0	1.35 (0.86, 2.12)
OR (95% CI), Model 4	1.0	0.85 (0.54, 1.34)	1.0	0.64 (0.38, 1.08)	1.0	2.49 (1.37, 4.54)	1.0	2.28 (1.39, 3.74)	1.0	0.80 (0.44, 1.45)	1.0	1.23 (0.48, 3.17)	1.0	1.45 (0.91, 2.29)

<sup>&</sup>lt;sup>a</sup>OR/95% CI, Odds Ratio, 95% Confidence Interval.

<sup>&</sup>lt;sup>b</sup>Model 1: Unadjusted crude model.

<sup>&</sup>lt;sup>c</sup>Model 2: Adjusted for use of other DS classes. <sup>d</sup>Model 3: Adjusted for total supplement use. <sup>e</sup>Model 4: Adjusted for other DS classes, total supplement use, age, gender, education, aerobic exercise, body mass index, and branch.

experiencing an adverse health event. Together, these findings suggest BMI may serve as a population risk factor for adverse health events associated with DS use and calls attention to the need to explore the relationship between health and behavioral habits which may exacerbate comorbidities.

Furthermore, our findings suggest demographic predictors of DS use, [2] including gender, age and degree of participation in aerobic exercise, do not increase the likelihood of experiencing a self-reported side-effect; thus consumption of specific DS ingredients may be the primary factor associated with occurrence of self-reported side-effects associated with use of multiple DS and supplements containing purported ergogenic components.

When examining associations between DS class and selfreported side-effects, users of protein supplements were more likely to report numbness/tingling. To our knowledge, numbness/tingling have only been previously associated with use of the amino acid beta-alanine. [20,21] Among protein supplement users, less than 1% reported using beta-alanine, and none of these individuals reported experiencing numbness/tingling; thus our findings suggest that other forms of protein or amino acid supplements may also result in paresthesia and thus warrants further investigation. Steroid use has previously been reported to result in a wide variety of severe adverse health effects; [22] however in the present study purported steroid analogues were only associated with greater likelihood of reporting dizziness. This form of DS class would be expected to be associated with a greater number of side-effects; however, there is a great deal of variability in the contents, dose and biological activity of these DS.

Since the Dietary Supplement Health and Education Act (DSHEA) of 1994 became law in the USA, availability of DS has steadily increased and approximately 85,000 unique products are currently on the market.<sup>[24]</sup> Since DSHEA does not require manufacturers to demonstrate safety and efficacy of their products, the findings of the present study suggest the need for a surveillance system capable of detecting side-effects of individual DS and interactions from use of combinations of DS. Minor adverse health events, such as abnormal heart beats and dizziness, may have effects on the safety of troops during combat situations and, as such, early detection of potentially harmful DS is necessary to ensure mission success is not compromised. Military personnel often do not have access to fresh food and as a result, supplementation may be necessary to help sustain warfighters during critical periods of energy restriction. Therefore, identifying supplements that are safe to consume and have scientificallyvalidated efficacy are critical for sustaining military health and performance. Given the extensive use of DS, especially use of performance-enhancing products by armed forces personnel, regular surveillance of this population may provide a means of detecting potentially harmful DS or combinations of DS before they are observed in the civilian population.

# **Limitations and strengths**

While the present analyses provide insight into DS use associated with self-reported symptoms, limitations should be acknowledged. As with all self-reported survey data, these data may be susceptible to report and recall bias. In addition, the association of DS use and self-reported side-effects was determined independently using separate questions on the survey questionnaire so the presence of a specific side-effect was not directly associated

with a specific DS. However, this provides the advantage of not suggesting to volunteers that a particular supplement produces specific side-effects. It should also be noted that the present study used a convenience sample which may have led to participation bias by inadvertently favoring inclusion of military personnel who maintain a strong belief in the use of DS. Given Department of Defense (DoD) regulations regarding the use of prohibited substances, including steroids and steroid analogues, we also acknowledge the potential for underreporting the use of this DS class, or any other DS, that could negatively impact career outcomes because their use could be viewed as a violation of rules regarding prohibited substances. Finally, in this study, prevalence of side-effects was not determined for the overall military population and as such, caution should be used when interpreting the findings. Despite these limitations, the strengths of the present study, including the use of multivariate analyses to control for demographic differences, DS class, and total supplement use, provide a means to draw initial insight into a potential health risk.

### Conclusion

In summary, use of more than one DS per week was associated with increased likelihood of reporting self-reported side-effects including abnormal heart beats, stomach pain, dizziness, tremors, and numbness/tingling. These self-reported side-effects are primarily associated with combination products containing multiple purported ergogenic aids. With the exception of BMI, previously identified demographic predictors of DS use were not associated with increased probability of reporting a side-effect. Findings of the present study confirm there is an increased likelihood of experiencing side-effects among individuals with a BMI of ≥30. Further research is necessary to understand the effects of multiple DS use and use of multi-component DS on an individual's health.

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# **Supporting information**

Additional supporting information may be found in the online version of this article at the publisher's web site.