

Supplemental Appendix Tables

Table A1 –Raw Data Sources and Relevant Corresponding Data Elements

Database	Date Range of Data	Relevant Data Elements
Drug Program Information Network (DPIN)	Apr. 1/2000 – Mar. 31/2016	Prescriptions for benzodiazepines (ATC codes N03AE, N05BA, N05CD), Z-Drugs (N05CF), Antidepressants, Antipsychotics, Mood stabilisers, Lithium and Opioids -Drug, dosage strength, dosage type, metric quantity dispensed, day supply, date of dispensation
Manitoba Health Insurance Registry	Apr. 1/1996 – Mar. 31/2016	Birth date/age of patient; sex; location of residence, marital status, date of Manitoba Health coverage, date of coverage end, reason for coverage end (i.e death, emigration etc.)
Medical Claims (Physician Billings)	Apr. 1/1996 – Mar. 31/2016	Services - type of physician (e.g., psychiatrist); dates of services, specific diagnoses (ICD-9 or ICD-10 equivalent)
Hospital Separations Abstracts	Apr. 1/1996 – Mar. 31/2016	Diagnoses (ICD-9 or ICD-10 equivalent), length of stay, admission dates, discharge dates,
Provider Registry/Physician Master File	Apr. 1/1996 – Mar. 31/2016	Physician Age, Sex, Specialty
Social Allowances Management Information Network (SAMIN)	Apr. 1/2001– Mar. 31/2013	Receipt of income assistance

Table A2 – International Classification for Disease Coding for Mood/Anxiety/Sleep Disorders (Cohort Inclusion)

	Source 1 - CPHA	Source 2 - MCHP	Study Algorithm

ICD Codes	<u>All Mental Health Disorders:</u> 9-CM: 290-319 10-CA: F00-F99	<u>Mood Disorders:</u> 296 and 311 (ICD-9-CM) or F30-F34, F39 (ICD 10-CA) <u>Anxiety Disorders:</u> 300 (ICD-9-CM) or F40-F42	<u>Mood disorders:</u> 296 and 311 (ICD-9-CM) or F30-F34, F39 (ICD 10-CA) <u>Anxiety disorders:</u> 300 (ICD-9-CM) or F40-F43 (ICD-10-CA) <u>Sleep disorders:</u> 307, 780 or F51, G47 (ICD-10-CA)
Case Definition	≥1 hospitalization or outpatient medical claim within 1 year	≥1 hospitalization or ≥1-3 outpatient medical claims within 3-5 years*	≥1 hospitalization or ≥3 outpatient medical claims within 5 years**

*Range of similar definitions between studies from 2000 to 2016

**The decision to use a 5-year pre-exposure window was based on the fact that all patients received a BZRA, which itself increases specificity for anxiety/sleep disorder diagnoses.

Table A3 – International Classification for Disease Coding Algorithms for Seizure, Cancer and Palliation (Cohort Exclusion)

	Seizure	Cancer and other Neoplasms	Palliation
ICD Codes	9-CM: 345 10-CA: G40	9-CM: 140-165, 170-176, 179-195, 200-208 10-CA: C00-C99	N/A*
Case Definition	≥1 hospitalization or ≥3 outpatient medical claim within 5 years before index date	≥1 hospitalization or ≥3 outpatient medical claims within 5 years before index date	Carrier code indicating palliative drug program enrollment in DPIN

*While ICD codes do exist for palliation, the DPIN carrier code '04' is expected to be a reliable indicator of when patients become ill enough that community use of medication is required for symptom management.

Table A4 – Independent ‘Patient’ Variables for Prediction of Long-Term BZRA Use

Baseline Patient Characteristics	Definition (Variable Type)	Measurement Period
Age	<i>3 age groups; 18-44, 45-64, 65+ (Ordinal)</i>	<i>Index Date</i>
Sex	<i>Male or Female (Dichotomous Categorical)</i>	<i>Index Date</i>
Region	<i>Urban; Winnipeg or Brandon postal-codes Rural; Any other Manitoba postal-code (Dichotomous Categorical)</i>	<i>Census Period closest in time to the index date</i>
Socioeconomic Status	<i>Socio-Economic Factor Index – Version 2 (SEFI-2) score composite of four variables based on geography; i) unemployment rate ii) average household income iii) proportion of single-parent households iv) proportion of population without high school education. Scores <0 indicate more favourable socioeconomic conditions Scores >0 indicate less ideal socioeconomic conditions (Ordinal Scale)</i>	<i>Census Period closest in time to the index date</i>
Income Assistance	<i>Record of income assistance (Dichotomous Categorical)</i>	<i>Up to 1-year before the Index Date</i>
Marriage Record	<i>Record of Marriage (Dichotomous Categorical)</i>	<i>Entire available registry period up to the Index Date</i>
Residential Mobility (i.e frequent mover)	<i>Average of 1 move every 3 years from beginning of registry coverage to index date (Dichotomous)</i>	<i>Entire available registry period up to the Index Date</i>
Comorbidity Burden	<i>Charlson Comorbidity Index (CCI) Score; 0, 1, 2+ (Ordinal Scale)</i>	<i>Up to 1-year before the Index Date</i>
Healthcare Resource Use	<i>Johns Hopkins Adjusted Clinical Groups Resource Utilization Band (Ordinal)</i>	<i>Up to 1-year before the Index Date</i>

	<i>Scale); placement into a band (0 to 5) based on grouping of ICD</i>	
Prescription Psychotropic Use (non-BZRA)	<i>Receipt of Prescription (Dichotomous Categorical)</i>	<i>Up to 1-year before the Index Date and 6 months after the Index Date</i>
Prescription Opioid Use	<i>Receipt of Prescription (Dichotomous Categorical)</i>	<i>Up to 1-year before the Index Date and 6 months after the Index Date</i>

Table A5 - Independent ‘First-Prescription’ Variables for Prediction of Long-Term BZRA Use

Characteristics of First Consultation and Subsequent Prescription	Definition	Measurement Period
Fiscal Year Period	<i>Fiscal year of first prescription Assigned to 3 five-year intervals; 2001-2005, 2006-2010, 2011-2015 (Ordinal)</i>	<i>Index Date</i>
Prescriber	<i>10 Years or More (Dichotomous)</i>	<i>Index Date</i>
Sex of Prescriber	<i>Male or Female (Dichotomous)</i>	<i>Index Date</i>
Prescriber Specialty	<i>General Practitioner, Psychiatry or Other (Categorical)</i>	<i>Index Date</i>

Table A6 – Logistic Regression Methodology

Criteria	Approach
Variable Selection	-Informal selection via published literature -Simple logistic regression; β values ($p < 0.25$)
Variable Coding	-Dichotomous Categorical; 0 or 1 -Ordinal; discrete number scale starting at 1 -Polychotomous Categorical; 0 or 1 with auto-generated dummy variables -No continuous variables retained
Events-per-Variable	-Minimum 10 events per independent variable rule
Conformity of Linear Gradient	-Ordered categorical variables assessed for conformity of linear gradient; nonconformity handled by variable transformation or separation into additional (design) variables (i.e fiscal year was shown to be linear with respect to outcome so condensed variable into 5-year increments)
Interaction effects	-Assessed at $p < 0.01$. Suspected interactions included; age*sex, residential mobility*SEFI*income assistance, psychotropic use*opioid use, RUB*CCI
Collinearity	-Analysis of variance inflation factor, correlation coefficients, eigenvalues -Significant collinearity; combine variables or removal of inferior explanatory variable
Statistical Significance	-Wald 95% CI for β and OR's
Goodness-of-Fit Measures	-C-statistic, Log-Likelihood Ratio, Hosmer-Lemeshow Statistic
Fitting Procedure	-Stepwise addition/subtraction of variables -Assessment of clinical significance

Table A7 – Goodness of Fit for Final Logistic Regression Models Predicting Long-Term Use of BZRA

Model	Model Type	Independent Variables	Likelihood Ratio (higher is better)	C statistic	Hosmer-Lemeshow Chi-Square Statistic
1	Main-Effects	9 Variables; Age-Sex Category, Period of First Rx, Psychotropic Use, Opioid Use, Income Assistance, Marriage, RUB CCI Score, Residential Mobility	6932 (p < 0.001)	0.738	10.78 (p = 0.215)
2	Main-Effects + Interaction Effects	10 Variables: All from Model 1 + Residential Mobility*Income Assistance	6945 (p < 0.001)	0.739	11.02 (p = 0.20)

Table A8 – Proportion of Long-Term BZRA Use by Differing Parameters and Duration Thresholds

Scenario*	Long-Term Use Parameter	Prescription Lapse Criteria	Patients (n)	Proportion of Cohort
A1**	First-Use Episode ≥ 180 days	30 days or 50% of previous Day Supply	9,327	4.51%
A2	First-Use Episode ≥ 90 days	30 days or 50% of previous Day Supply	13,745	6.64%
A3	First-Use Episode ≥ 60 days	30 days or 50% of previous Day Supply	19,948	9.64%
A4	First-Use Episode ≥ 180 days	60 Days or 50% of previous Day Supply	13,050	6.31%
A5	First-Use Episode ≥ 180 days	90 Days	16,831	8.13%
A6	First-Use Episode ≥ 270 days	90 Days	15,214	7.35%
A7	First-Use Episode ≥ 365 days	90 Days	14,219	6.87%
B1	Mean Episode Duration ≥ 180 days	30 days or 50% of previous Day Supply	38,853	18.78%
B2	Mean Episode Duration ≥ 90 days	30 days or 50% of previous Day Supply	58,442	28.24%
B3	Mean Episode Duration ≥ 60 days	30 days or 50% of previous Day Supply	72,639	35.10%
B4	Mean Episode Duration ≥ 180 days	60 Days or 50% of previous Day Supply	44,593	21.55%
B5	Mean Episode Duration ≥ 180 days	90 Days	50,142	24.23%
B6	User Mean Episode Duration ≥ 270 days	90 Days	39,395	19.04%
B7	User Mean Episode Duration ≥ 365 days	90 Days	32,200	15.56%

*A=First Episode Scenario; B=Mean Episode Duration Scenario

**Primary Scenario Used for Logistic Regression

Table A9 - Proportion of Long-Term Z-Drug Use by Differing Parameters and Duration Thresholds

Scenario	Long-Term Use Parameter	Prescription Lapse Criteria	Patients (n)	Proportion of Sub-Cohort
A1	First-Use Episode \geq 180 days	30 days or 50% of previous Day Supply	8,206	7.41%
A2	First-Use Episode \geq 90 days	30 days or 50% of previous Day Supply	12,155	11.0%
A3	First-Use Episode \geq 60 days	30 days or 50% of previous Day Supply	17,126	15.5%
A4	First-Use Episode \geq 180 days	60 Days or 50% of previous Day Supply	10,437	9.43%
A5	First-Use Episode \geq 180 days	90 Days	12,719	11.49%
A6	First-Use Episode \geq 270 days	90 Days	11,117	10.04%
A7	First-Use Episode \geq 365 days	90 Days	10,045	9.07%
B1	User Mean Episode Duration \geq 180 days	30 days or 50% of previous Day Supply	21,859	19.75%
B2	User Mean Episode Duration \geq 90 days	30 days or 50% of previous Day Supply	32,020	28.92%
B3	User Mean Episode Duration \geq 60 days	30 days or 50% of previous Day Supply	39,690	35.85%
B4	User Mean Episode Duration \geq 180 days	60 Days or 50% of previous Day Supply	24,098	21.77%
B5	User Mean Episode Duration \geq 180 days	90 Days	26,477	23.92%
B6	User Mean Episode Duration \geq 270 days	90 Days	21,040	19.01%
B7	User Mean Episode Duration \geq 365 days	90 Days	17,358	15.68%

Table A10 – Patient Characteristics of Z-Drug Users by First Use Episode Duration

		Short-term	Long-term	Total
Number of Users		102,459 (100%)	8,204 (100%)	110,663 (100%)
<i>Sex Distribution</i>	<i>Male</i>	40,516 (39.5%)	3,473 (42.3%)	43,989 (39.8%)
	<i>Female</i>	61,943 (60.5%)	4,731 (57.7%)	66,674 (60.2%)
<i>Age Category</i>	<i>18-44</i>	42,663 (41.6%)	1,795 (21.9%)	44,458 (40.2%)
	<i>45-64</i>	39,817 (38.9%)	3,184 (38.8%)	43,001 (38.9%)
	<i>65+</i>	20,011 (19.5%)	3,227 (39.3%)	23,238 (21.0%)
<i>SEFI-2 Score</i>	<i><-1</i>	13,678 (13.3%)	981 (12.0%)	14,659 (13.2%)
	<i>-1 to 0</i>	45,136 (44.1%)	3,674 (44.8%)	48,810 (44.1%)
	<i>0 to 1</i>	33,719 (32.9%)	2,885 (35.2%)	36,604 (33.1%)
	<i>>1</i>	9,958 (9.7%)	666 (8.1%)	10,624 (9.6%)
<i>Residence Distribution</i>	<i>Urban</i>	63,207 (61.7%)	3,313 (40.4%)	66,520 (60.1%)
	<i>Rural</i>	39,284 (38.3%)	4,893 (59.6%)	44,177 (39.9%)
<i>High Residential Mobility</i>		22,408 (21.9%)	2,523 (30.8%)	24,931 (22.5%)
<i>Receipt of Income Assistance</i>		8,351 (8.2%)	758 (9.2%)	9,109 (8.2%)
<i>Marriage Record</i>		57,308 (55.9%)	4,595 (56.0%)	61,903 (55.9%)
<i>Johns Hopkins Healthcare Resource Utilization Band</i>	<i>0 (no utilization)</i>	1,771 (1.7%)	234 (2.9%)	2,005 (1.8%)
	<i>1</i>	3,205 (3.1%)	175 (2.1%)	3,380 (3.1%)
	<i>2</i>	17,523 (17.1%)	1,012 (12.3%)	18,535 (16.7%)
	<i>3</i>	65,067 (63.5%)	4,699 (57.3%)	69,766 (63.0%)
	<i>4</i>	10,810 (10.6%)	1,259 (15.3%)	12,069 (10.9%)
	<i>5 (high-utilization)</i>	4,083 (4.0%)	825 (10.1%)	4,908 (4.4%)

		Short-term	Long-term	Total
Number of Users		102,459 (100%)	8,204 (100%)	110,663 (100%)
<i>Charlson Comorbidity index Score</i>	0	72,490 (70.8%)	4,528 (55.2%)	77,018 (69.6%)
	1	19,495 (19.0%)	1,905 (23.2%)	21,400 (19.3%)
	2+	10,506 (10.3%)	1,773 (21.6%)	12,279 (11.1%)
<i>Non-BZRA Psychotropic Prescription Dispensations</i>	0	27,797 (27.1%)	1,784 (21.7%)	29,581 (26.7%)
	1	36,939 (36.1%)	2,156 (26.3%)	39,095 (35.3%)
	2+	37,755 (36.8%)	4,266 (52.0%)	42,021 (38.0%)
<i>Opioid Prescription Dispensations</i>	0	47,427 (46.3%)	3,298 (40.2%)	50,725 (45.8%)
	1	34,505 (33.7%)	2,772 (33.8%)	37,277 (33.7%)
	2+	20,559 (20.1%)	2,136 (26.0%)	22,695 (20.5%)
<i>Sex of Prescriber Issuing First Prescription</i>	Male	71,485 (69.8%)	5,627 (68.6%)	77,112 (69.7%)
	Female	28,485 (27.8%)	2,273 (27.7%)	30,758 (27.8%)
<i>Age of Prescriber Issuing First Prescription</i>	50+ Years	47,871 (46.7%)	4,014 (48.9%)	51,885 (46.9%)
	<50 Years	49,257 (48.1%)	3,758 (45.8%)	53,015 (47.9%)
<i>Type of Prescriber Issuing First Prescription</i>	General Practitioner	78,610 (76.7%)	6,366 (77.6%)	84,976 (76.8%)
	Psychiatry	3,912 (3.8%)	475 (5.8%)	4,387 (4.0%)
	Other	3,881 (3.8%)	381 (4.6%)	4,262 (3.9%)
<i>Period of First Prescription</i>	2001-2006	34,360 (33.5%)	1,526 (18.6%)	35,886 (32.4%)
	2006-2011	37,752 (36.8%)	2,808 (34.2%)	40,560 (36.7%)
	2011-2016	30,379 (29.6%)	3,872 (47.2%)	34,251 (31.0%)

Table A11 – Frequency of Charlson Comorbidity Group Diagnoses by First Use Episode Duration for Z-Drug Cohort

Charlson Diagnosis	Short-Term ‘First-Episode’ Users (n=102,459)	Long-Term ‘First-Episode’ Users (n=8,204)	Z-Test of Two Proportions
Myocardial Infarction	1,836 (1.8%)	306 (3.7%)	p < 0.01
Congestive Heart Failure	3,174 (3.1%)	700 (8.5%)	p < 0.01
Peripheral Vascular Disease	1,772 (1.7%)	284 (3.5%)	p < 0.01
Cerebrovascular Disease	2,321 (2.3%)	550 (6.7%)	p < 0.01
Dementia	1,925 (1.9%)	865 (10.5%)	p < 0.01
COPD	12,357 (12.1%)	1,171 (14.3%)	p < 0.01
Connective Tissue/Rheumatic Disease	1,906 (1.9%)	243 (3.0%)	p < 0.01
Peptic Ulcer Disease	1,111 (1.1%)	123 (1.5%)	p < 0.01
Mild Liver Disease	1,672 (1.6%)	139 (1.7%)	p = 0.33
Moderate/Severe Liver Disease	275 (0.2%)	38 (0.4%)	p < 0.01
Uncomplicated Diabetes	9,317 (9.1%)	1,150 (14.0%)	p < 0.01
Complicated Diabetes	1,639 (1.6%)	328 (4.0%)	p < 0.01
Paraplegia and Hemiplegia	508 (0.5%)	136 (1.7%)	p < 0.01
Renal Disease	1,543 (1.5%)	293 (3.6%)	p < 0.01
Cancer	2,109 (2.1%)	247 (3.0%)	p < 0.01
Metastatic Carcinoma	429 (0.4%)	45 (0.5%)	p = 0.04
HIV/AIDS	118 (0.1%)	16 (0.2%)	p = 0.02

Table A12 – Statistical Associations between Predictor Variables and Long-term Use of Z-Drugs

Independent Variable		Use Duration					
		≥180 days		≥90 days		≥60 days	
		<i>Crude OR (95% CI)</i>	<i>Adjusted OR (95% CI)</i>	<i>Crude OR (95% CI)</i>	<i>Adjusted OR (95% CI)</i>	<i>Crude OR (95% CI)</i>	<i>Adjusted OR (95% CI)</i>
<i>Male</i>		1.12 (1.07-1.18)	1.04 (0.99-1.09)	1.13 (1.08-1.17)	1.05 (1.01-1.10)	1.08 (1.05-1.12)	1.04 (1.00-1.08)
<i>Age</i>	<i>18-44</i>	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	<i>45-64</i>	1.90 (1.79-2.02)	2.02 (1.89-2.17)	1.74 (1.66-1.82)	1.78 (1.68-1.88)	1.71 (1.64-1.78)	1.68 (1.60-1.76)
	<i>65+</i>	3.83 (3.61-4.07)	3.71 (3.44-4.00)	3.24 (3.08-3.40)	3.08 (2.90-3.28)	2.99 (2.87-3.12)	2.78 (2.64-2.93)
<i>Rural Residence</i>		0.92 (0.88-0.96)	1.13 (1.07-1.19)	0.99 (0.96-1.03)	1.02 (0.98-1.07)	1.08 (1.04-1.11)	0.95 (0.91-0.99)
<i>High Residential Mobility</i>		1.59 (1.51-1.67)	1.26 (1.19-1.33)	1.53 (1.46-1.59)	1.21 (1.15-1.27)	1.30 (1.26-1.35)	1.12 (1.07-1.17)
<i>Income Assistance</i>		1.15 (1.06-1.24)	1.47 (1.34-1.61)	1.02 (0.95-1.09)	1.29 (1.19-1.40)	0.82 (0.77-0.87)	1.08 (1.00-1.17)
<i>SEFI-2 Score</i>	<i><-1</i>	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	<i>-1 to 0</i>	1.14 (1.06-1.22)	1.07 (0.99-1.16)	1.03 (0.97-1.09)	0.98 (0.92-1.04)	0.95 (0.91-1.00)	0.94 (0.89-0.99)
	<i>0 to 1</i>	1.19 (1.11-1.29)	1.08 (0.99-1.17)	1.04 (0.98-1.11)	0.99 (0.93-1.06)	0.92 (0.87-0.97)	0.93 (0.88-0.99)
	<i>>1</i>	0.93 (0.84-1.03)	0.84 (0.75-0.94)	0.80 (0.73-0.87)	0.77 (0.70-0.85)	0.68 (0.63-0.73)	0.72 (0.66-0.78)
<i>Married</i>		1.00 (0.96-1.05)	0.86 (0.82-0.91)	1.07 (1.03-1.10)	0.93 (0.89-0.98)	1.13 (1.10-1.17)	0.98 (0.94-1.01)
<i>Opioid Use</i>		1.28 (1.22-1.34)	1.15 (1.09-1.21)	1.26 (1.21-1.31)	1.15 (1.11-1.20)	1.18 (1.14-1.21)	1.11 (1.07-1.15)

Independent Variable		Use Duration					
		≥180 days		≥90 days		≥60 days	
		<i>Crude OR (95% CI)</i>	<i>Adjusted OR (95% CI)</i>	<i>Crude OR (95% CI)</i>	<i>Adjusted OR (95% CI)</i>	<i>Crude OR (95% CI)</i>	<i>Adjusted OR (95% CI)</i>
<i>Psychotropic Rx Use (Non-BZRA)</i>		1.34 (1.27-1.41)	1.24 (1.17-1.32)	1.35 (1.29-1.41)	1.27 (1.20-1.33)	1.22 (1.17-1.27)	1.19 (1.14-1.24)
<i>Charlson Comorbidity Index Score</i>	0	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	1	1.56 (1.48-1.65)	1.25 (1.18-1.33)	1.45 (1.39-1.52)	1.21 (1.15-1.27)	1.33 (1.28-1.38)	1.13 (1.08-1.19)
	2+	2.70 (2.55-2.87)	1.46 (1.36-1.58)	2.34 (2.22-2.46)	1.38 (1.29-1.47)	2.02 (1.93-2.12)	1.30 (1.22-1.37)
<i>Resource Utilization Band</i>	0-3 (<i>≤Moderate</i>)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	4 (<i>High</i>)	1.67 (1.56-1.78)	1.16 (1.08-1.25)	1.47 (1.39-1.56)	1.09 (1.01-1.16)	1.30 (1.24-1.37)	1.00 (0.95-1.07)
	5 (<i>Very High</i>)	2.89 (2.67-3.13)	1.55 (1.41-1.70)	2.43 (2.26-2.61)	1.42 (1.30-1.55)	1.97 (1.85-2.11)	1.22 (1.12-1.32)
<i>Male Prescriber of First Prescription</i>		0.99 (0.94-1.04)	0.97 (0.92-1.03)	0.98 (0.94-1.02)	0.98 (0.93-1.02)	0.94 (0.90-0.97)	0.93 (0.90-0.97)
<i>Prescriber Age ≥50 Years</i>		1.10 (1.05-1.15)	0.98 (0.93-1.03)	1.10 (1.06-1.15)	0.98 (0.94-1.02)	1.15 (1.11-1.19)	1.05 (1.01-1.09)
<i>Prescriber of First Prescription</i>	GP	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	Psychiatrist	1.50 (1.36-1.66)	1.96 (1.76-2.17)	1.36 (1.25-1.49)	1.72 (1.57-1.89)	1.11 (1.02-1.20)	1.38 (1.27-1.51)
	Other	1.21 (1.09-1.35)	0.92 (0.82-1.03)	1.18 (1.07-1.29)	0.91 (0.83-1.00)	1.19 (1.10-1.29)	0.98 (0.91-1.07)
<i>Period of First Prescription</i>	2001-2006	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	2006-2011	1.68 (1.57-1.79)	1.57 (1.46-1.68)	1.67 (1.59-1.76)	1.56 (1.47-1.66)	1.53 (1.46-1.60)	1.46 (1.39-1.54)
	2011-2015	2.87 (2.70-3.05)	2.45 (2.28-2.65)	2.83 (2.69-2.97)	2.44 (2.30-2.59)	2.20 (2.10-2.29)	1.96 (1.86-2.07)

