ONLINE SUPPLEMENT

Section 1: Listing and brief description of other health administrative databases used

a. Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD) - contains information on all hospital admissions

b. ICES congestive heart failure (CHF) database - contains individuals with validated physician-diagnosed CHF [1]

c. ICES hypertension database - contains individuals with validated physician-diagnosed hypertension [2]

d. National Ambulatory Care Reporting System - contains information on all emergency room (ER) visits

e. Ontario Cancer Registry - a validated provincial cancer registry [3]

f. Ontario Diabetes Database - contains individuals with validated physician-diagnosed diabetes [4]

g. Ontario Health Insurance Plan (OHIP) database - contains information on all patient contact with physicians in both ambulatory and hospital settings

h. Ontario Mental Health Reporting System (OMHRS) - contains information on all mental health hospital admissions

i. Office of the Registrar General - Deaths (ORGD) - contains information on cause of death

j. Registered Persons Database - contains demographic information and date of death (if available) of all Ontarians

k. Same-Day Surgery database - contains information on surgical procedures not requiring overnight hospital stays

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Section 2: Baseline characteristics of community-dwelling cohort, before and after propensity score matching (full list of covariates included in the propensity score model[a])

	Before propensity score matching			After propensity score matching		
	New SSRI/SNRI users	**Non-SSRI/ SNRI users**	**Standardized difference[b]**	**New SSRI/SNRI users**	**Non-SSRI/SNRI users**	**Standardized difference[b]**
	N=29,835	N=88,776		N=28,360	N=28,360	
Age (mean + SD)	77.4 ± 7.2	76.9 ± 7.5	0.07	77.4 ± 7.2	77.5 ± 7.7	0.01
% female	55.7%	44.9%	0.22	54.6%	54.5%	0.0006
Low income as per ODB flag (%)	24.0%	20.6%	0.08	23.6%	23.6%	0.0001
Income quintile (%)						
1 (lowest)	24.4%	22.9%	0.04	24.3%	24.6%	0.006
2	22.1%	22.1%	0.0008	22.1%	21.9%	0.005
3	19.1%	19.6%	0.01	19.1%	19.0%	0.003
4	17.9%	18.6%	0.02	18.1%	18.1%	0.0005
5 (highest)	16.1%	16.4%	0.01	16.1%	16.2%	0.002
Missing data	0.4%	0.4%	0.005	0.4%	0.4%	0.001
% rural setting	17.2%	16.9%	0.008	17.1%	17.3%	0.003
COPD exacerbation frequency past year (%)						
0	58.1%	61.5%	0.07	58.6%	58.6%	0
>=1 outpatient exacerbation	17.2%	18.5%	0.03	17.1%	17.1%	0
>=1 exacerbation requiring hospital presentation	24.7%	20.0%	0.11	24.2%	24.2%	0
COPD exacerbation in the past 30 days (%)	9.9%	10.9%	0.03	10.0%	9.8%	0.004
Duration of COPD year prior (%)						
< 2 years	20.8%	32.6%	0.27	21.7%	22.1%	0.009
2-5 years	18.6%	17.4%	0.03	18.8%	18.5%	0.006
> 5 years	60.6%	50.0%	0.21	59.5%	59.4%	0.003

Table continued from previous page						
	Before propensity score matching			**After propensity score matching**		
	New SSRI/SNRI users	**Non-SSRI/ SNRI users**	**Standardized difference[b]**	**New SSRI/SNRI users**	**Non-SSRI/SNRI users**	**Standardized difference[b]**
	N=29,835	N=88,776		N=28,360	N=28,360	
Respiratory medications in the past 6 months (%)						
Short/long-acting beta agonists	40.3%	36.4%	0.08	39.7%	39.4%	0.007
Short/long-acting anticholinergics	41.2%	39.2%	0.04	40.8%	40.8%	0.0003
Inhaled corticosteroids	12.3%	12.1%	0.006	12.3%	12.3%	0.002
Combination inhaled corticosteroid-long acting beta agonist inhalers	36.4%	33.2%	0.07	35.9%	35.8%	0.002
Oral corticosteroids	17.8%	13.9%	0.11	17.3%	17.1%	0.003
Theophylline	2.2%	1.8%	0.03	2.2%	2.2%	0.003
Respiratory antibiotics	48.1%	44.3%	0.08	47.5%	47.5%	0.0003
Total number of outpatient visits in the past 12 months (mean + SD)	16.2 ± 11.6	13.9 ± 10.0	0.21	15.9 ± 11.5	15.9 ± 10.9	0.0003
Total number of hospitalizations in the past 12 months (mean + SD)	0.7 ± 1.1	0.5 ± 0.9	0.20	0.6 ± 1.1	0.6 ± 1.1	0.005
Any ICU admission in the past 12 months (%)	9.9%	7.5%	0.08	9.6%	9.6%	0.0002
Any surgery in the past 12 months (%)	10.3%	9.1%	0.04	10.0%	10.0%	0.0007
Johns Hopkins Adjusted Clinical Group[c] (%)						
Bottom tertile	27.2%	39.2%	0.26	28.2%	28.0%	0.004
Middle tertile	27.5%	29.2%	0.04	27.8%	27.9%	0.001
Top tertile	45.3%	31.5%	0.29	44.0%	44.1%	0.003

Table continued from previous page						
	Before propensity score matching			After propensity score matching		
	New SSRI/SNRI users	Non-SSRI/ SNRI users	Standardized difference[b]	New SSRI/SNRI users	Non-SSRI/SNRI users	Standardized difference[b]
	N=29,835	N=88,776		N=28,360	N=28,360	
Non-COPD pulmonary disease[d] (%)	50.5%	46.9%	0.07	50.2%	50.0%	0.004
Ischemic heart disease[d] (%)	35.7%	33.5%	0.05	35.4%	35.7%	0.005
Congestive heart failure[d] (%)	30.0%	27.5%	0.06	29.8%	30.3%	0.01
ER visit/hospitalization for ischemic heart disease or congestive heart failure in the year prior (%)	16.5%	13.1%	0.09	16.1%	16.1%	0.002
Hypertension[d] (%)	81.2%	78.8%	0.06	81.1%	81.2%	0.005
Atherosclerosis[d] (%)	7.7%	7.4%	0.01	7.7%	7.7%	0.002
Diabetes[d] (%)	34.8%	33.7%	0.02	34.7%	35.3%	0.01
Previous stroke and cerebrovascular disease[d] (%)	15.6%	11.4%	0.13	15.1%	15.2%	0.001
Cancer[d] (%)	23.3%	24.9%	0.04	23.5%	23.7%	0.004
Musculoskeletal or connective tissue disease[d] (%)	93.4%	89.6%	0.14	93.2%	93.2%	0.001
Osteoporosis[d] (%)	17.1%	14.7%	0.06	16.9%	16.8%	0.004
Psychotic psychiatric disease[d,e] (%)	9.5%	4.2%	0.21	8.5%	8.4%	0.005
Non-psychotic psychiatric disease[d,f] (%)	75.9%	42.9%	0.71	74.7%	74.8%	0.004

Table continued from previous page						
	Before propensity score matching			**After propensity score matching**		
	New SSRI/SNRI users	**Non-SSRI/ SNRI users**	**Standardized difference[b]**	**New SSRI/SNRI users**	**Non-SSRI/SNRI users**	**Standardized difference[b]**
	N=29,835	N=88,776		N=28,360	N=28,360	
Sleep disorder[d] (%)	60.1%	55.1%	0.10	59.9%	60.1%	0.004
Total number of non-SSRI/SNRI drugs received in the past year (mean + SD)	13.8 ± 6.8	11.4 ± 6.1	0.37	13.5 ± 6.6	13.5 ± 6.6	0.004
Benzodiazepine in the past 6 months (%)	38.3%	17.9%	0.47	35.6%	35.4%	0.004
Oral/transdermal opioid in the past 6 months (%)	35.1%	22.5%	0.28	33.3%	33.1%	0.004
Smoking cessation drug[g] in the past 12 months (%)	2.9%	1.7%	0.08	2.6%	2.5%	0.007
Spirometry in the past 12 months (%)	26.7%	28.5%	0.04	26.8%	26.5%	0.005
% cohort entry in flu season[h]	38.5%	37.0%	0.03	38.2%	38.2%	0.0004

ER = emergency room; ODB = Ontario Drug Benefit; SD = standard deviation

[a]An abridged version of this table is found in the manuscript proper.

[b]Standardized differences of > 0.10 are thought to indicate potentially meaningful differences.

[c]This is a measure of patient morbidity burden, using hospitalization and ambulatory visit data based on a 2-year look-back from the index date. The Johns Hopkins ACG(r) System Ver XX.

[d]Presence of comorbidities was based on 5-year look-back from the index date.

[e]Includes schizophrenia, bipolar disorder and paranoid states.

[f]Includes depression disorders, anxiety disorders, phobias, stress disorders, dissociative and somatization disorders, eating disorders, personality disorders, mental and behavioural disorders due to substance abuse, and tic disorders.

[g]Includes Wellbutrin and Varenicline.

[h]Defined as November 1 to March 31.

Section 3: Additional sensitivity analyses for community-dwelling cohort

Methods for additional sensitivity analyses

Several additional sensitivity analyses were performed. First, we evaluated our outcomes distinguishing by whether a new SSRI or a new SNRI drug was received. The purpose of this analysis was to examine for possible drug class effects, since SSRI and SNRI drugs have differing neurotransmitter reuptake selectivities [1] and these differences may influence respiratory outcome risk. For example, SSRI drugs have more serotonin reuptake selectivity than SNRI drugs [1] and serotonin has been linked to reduced apoptotic cells clearance [2], which may in turn increase airway tract inflammation and plugging, and thereby, chances for respiratory tract infection [3].

Second, among individuals receiving citalopram (which was found to be the most commonly dispensed SSRI/SNRI, received by 35.2% of community-dwelling new SSRI/SNRI users and 48.0% of long term care resident new SSRI/SNRI users), we evaluated our outcomes by citalopram daily dose to examine for a possible dose-response relationship and to determine if adverse event risk possibly extended to 'lower dose' levels. We limited this sensitivity analysis to citalopram users, since this was the most commonly dispensed SSRI/SNRI drug and since it was not possible to convert the eight different SSRI/SNRI drugs covered by the Ontario Drug Benefit (ODB) program into 'milligram equivalents' of a single drug formulation. We considered two different citalopam dose levels: <20 mg/day (lower dose) and >=20 mg/day (higher dose). A threshold of 20 mg/day was chosen to distinguish 'lower' versus 'higher' citalopram daily dose levels, since the number of drug recipients was roughly evenly split above and below this threshold.

We previously reported that, among older adults with COPD, new use of another psychoactive medication class (benzodiazepine agonists) was associated with increased risk for adverse respiratory events [4]. Therefore, we performed a final sensitivity analysis where we evaluated our outcomes among new SSRI/SNRI drug users, but with the control group limited to new benzodiazepine users, in order to compare the respiratory safety profile of SSRI/SNRI drugs to benzodiazepines. New benzodiazepine use was defined as a dispensing for a benzodiazepine drug, with no benzodiazepine drug receipt in the year prior. For this sensitivity analysis, we excluded concomitant benzodiazepine users from the exposed group and concomitant SSRI/SNRI users from the control group, in order to minimize group contamination. Using a similar approach as previous [5], we defined concomitant use of either drug as receipt of the respective drug within 90 days prior to the index date. The propensity score was re-estimated for this specific sensitivity analysis, since a new control definition was used.

A final sensitivity analysis was performed where we evaluated our outcomes among new SSRI/SNRI drug users, but with the control group limited to new tricyclic antidepressant users. Tricyclic antidepressants, like SSRI/SNRI drugs, have serotonergic reuptake activity (albeit weaker) and the purpose of this sensitivity analysis was to examine whether risk of adverse respiratory events would be higher with receipt of the more serotonergic SSRI/SNRI drugs. New tricyclic antidepressant use was defined as a dispensing for a tricyclic antidepressant, with no tricyclic antidepressant drug receipt in the year prior. For this sensitivity analysis, we excluded concomitant tricyclic antidepressant users from the exposed group and concomitant SSRI/SNRI users from the control group, in order to minimize group contamination. Using a similar approach as previous [5], we defined concomitant use of either drug as receipt of the respective drug within 90 days prior to the index date. Because we observed that there were more exposed

than control individuals in this sensitivity analysis, we elected to balance the two groups on measured covariates using inverse probability of treatment weighting (IPTW) using the propensity score [6-7] (rather than using propensity score matching methods), in order to minimize loss of exposed individuals.

Results and discussion of additional sensitivity analyses

By SSRI versus SNRI drug class. Individuals receiving a new SSRI drug versus controls had significantly increased rates of hospital admission for COPD or pneumonia (HR 1.20; 95% CI 1.09-1.32), ER visits for COPD or pneumonia (HR 1.14; 95% CI 1.03-1.27), COPD or pneumonia-related mortality (HR 1.35; 95% CI 1.08-1.69) and all-cause mortality (HR 1.26; 95% CI 1.16-1.38), but significantly decreased rate of outpatient exacerbation (HR 0.90; 95% CI 0.85-0.96) (Table 1 in this section). There were no significant associations observed between new SNRI drug receipt and any of our outcomes. While these results suggest that it is drugs with greater serotonin reuptake selectivity that predispose to increased risk for adverse respiratory outcomes, the SNRI user subgroup may have been under-powered to detect for potentially significant results, as far fewer individuals in the exposed group received SNRI drugs versus SSRI drugs (SNRI recipients comprised 20.9% of new SSRI/SNRI drug users in the community-dwelling cohort).

By citalopram daily dose category. Individuals receiving lower daily doses of citalopram compared to controls had significantly increased rates of hospital admission for COPD or pneumonia (HR 1.45; 95% CI 1.20-1.74), COPD or pneumonia-related mortality (HR 2.31; 95% CI 1.40-3.81) and all-cause mortality (HR 1.48; 95% CI 1.26-1.75) (Table 2 in this

section). Significantly increased rate of all-cause mortality was observed among individuals receiving higher daily doses of citalopram compared to controls (HR 1.25; 95% CI 104-1.51). No other significant associations were observed in either group. The fact that increased rates of adverse respiratory outcomes were observed among individuals receiving lower daily doses of citalopram indicates that potential respiratory safety concerns regarding SSRI/SNRI drug use in COPD extend to lower drug dose levels. The finding of a greater number of 'positive results' in the lower versus higher daily citalopram dose category, and the finding of a higher HR for all-cause mortality in the lower versus higher daily citalopram dose group, suggests residual confounding may be effecting the results. However, the aforementioned findings may also reflect that our drug dose categorization was not fully accurate. A minority of individuals in both drug dose groups were simultaneously receiving more than one SSRI/SNRI drug, and this occurred more frequently in the lower (6.6%) versus higher (3.0%) citalopram dose group. It was not possible to convert other concomitant SSRI/SNRI drug use, when present, into 'citalopram milligram equivalents' and this limitation results in some degree of drug dose categorization inaccuracy.

With new benzodiazepine users serving as controls. Compared to new benzodiazepine users, new SSRI/SNRI users had significantly decreased rates of outpatient exacerbation (HR 0.82; 95% CI 0.76-0.89), COPD or pneumonia-related mortality (HR 0.75; 95% CI 0.59-0.94) and all-cause mortality (HR 0.75; 95% CI 0.68-0.82) (Table 3 in this section). No other significant associations were found. Although both new SSRI/SNRI drug use and new benzodiazepine drug use [4] are independently associated with increased adverse respiratory risk when compared to new, but non-specific, drug receipt in the older adult COPD population, the

results of this sensitivity analysis suggest that benzodiazepine drugs predispose to greater adverse respiratory risk than SRRI/SNRI drugs when compared head-to-head.

With new tricyclic antidepressant users serving as controls. Compared to new tricyclic antidepressant users, new SSRI/SNRI users had significantly increased rates of hospital admission for COPD or pneumonia (HR 1.18; 95% CI 1.03-1.37), COPD or pneumonia-related mortality (HR 1.57; 95% CI 1.07-1.29) and all-cause mortality (HR 1.39; 95% CI 1.22-1.59) (Table 4 in this section). No other significant associations were found. These findings suggest that it is the serotonergic activity of SSRI/SNRI drugs (which is present to a greater degree in these medications compared to tricyclic antidepressants) that is responsible for increased risk of adverse respiratory outcomes.

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Table 1. Hazard ratios and confidence intervals for outcomes in the community-dwelling propensity matched cohort, distinguishing by SSRI/SNRI drug type received

SSRI/SNRI drug type received	SSRI/SNRI status	Outpatient exacerbation		ER visit outcome		Hospital admission outcome		ICU outcome		COPD or pneumonia-related mortality		All-cause mortality	
		N (%)	HR (95% CI, p-value)	N (%)	HR (95% CI, p-value)	N (%)	HR (95% CI, p-value)	N (%)	HR (95% CI, p-value)	N (%)	HR (95% CI, p-value)	N (%)	HR (95% CI, p-value)
SSRI drugs	New users	1903 (8.5%)	0.90 (0.85-0.96), 0.0009	737 (3.3%)	1.14 (1.03-1.27), 0.01	922 (4.1%)	1.20 (1.09-1.32), 0.0001	131 (0.6%)	1.15 (0.89-1.48), 0.28	178 (0.8%)	1.35 (1.08-1.69), 0.009	1163 (5.2%)	1.26 (1.16-1.38), <0.0001
	Non- users	2088 (9.3%)		645 (2.9%)		769 (3.4%)		114 (0.5%)		133 (0.6%)		929 (4.1%)	
SNRI drugs	New users	505 (8.6%)	0.94 (0.84-1.06), 0.33	181 (3.1%)	1.08 (0.88-1.33), 0.47	183 (3.1%)	0.93 (0.76-1.12), 0.44	23 (0.4%)	0.77 (0.44-1.32), 0.34	26 (0.4%)	0.87 (0.51-1.47), 0.60	193 (3.3%)	0.91 (0.75-1.11), 0.35
	Non- users	531 (9.0%)		168 (2.8%)		197 (3.3%)		30 (0.5%)		30 (0.5%)		212 (3.6%)	

Table 2. Hazard ratios and confidence intervals for outcomes in the community-dwelling propensity matched cohort, distinguishing by citalopram daily dose

Citalo-pram daily dose	SSRI/ SNRI status	Outpatient exacerbation		ER visit for COPD or pneumonia		Hospital admission COPD or pneumonia		ICU admission during a hospitalization for COPD or pneumonia		COPD or pneumonia-related mortality		All-cause mortality	
		N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value
Lower dose (< 20 mg/day)	New users	449 (8.4%)	0.93 (0.82-1.06), 0.29	175 (3.3%)	1.08 (0.88-1.33), 0.47	267 (5.0%)	1.45 (1.20-1.74), 0.0001	25 (0.5%)	0.78 (0.46-1.32), 0.35	50 (0.9%)	2.31 (1.40-3.81), 0.001	335 (6.3%)	1.48 (1.26-1.75), <0.0001
	Non-users	477 (8.9%)		162 (3.0%)		186 (3.5%)		32 (0.6%)		22 (0.4%)		229 (4.3%)	
Higher dose (>=20 mg/day)	New users	380 (8.2%)	0.93 (0.81-1.07), 0.30	146 (3.1%)	1.01 (0.80-1.26), 0.95	184 (4.0%)	1.14 (0.93-1.40), 0.20	31 (0.7%)	1.41(0.82-2.44), 0.22	33 (0.7%)	0.83 (0.52-1.32), 0.44	246 (5.3%)	1.25 (1.04-1.51), 0.02
	Non-users	406 (8.7%)		145 (3.1%)		162 (3.5%)		22 (0.5%)		40 (0.9%)		198 (4.3%)	

Table 3. Hazard ratios and confidence intervals for outcomes in the community-dwelling propensity matched cohort, where the control group was new benzodiazepine drug users

Outcomes	Status of SSRI/SNRI use	Number of events (%)	HR (95% CI, p-value)
Outpatient respiratory exacerbation	New SSRI or SNRI users	1175(7.8%)	0.82 (0.76-0.89), <0.0001
	New benzodiazepine users	1410(9.4%)	referent
ER visit for COPD or pneumonia	New SSRI or SNRI users	449(3.0%)	0.91 (0.80-1.03), 0.13
	New benzodiazepine users	495(3.3%)	referent
Hospital admissions COPD or pneumonia	New SSRI or SNRI users	579(3.9%)	1.01 (0.90-1.13), 0.86
	New benzodiazepine users	573(3.8%)	referent
ICU admission during a hospitalization for COPD or pneumonia	New SSRI or SNRI users	76(0.5%)	0.96 (0.70-1.32), 0.81
	New benzodiazepine users	79(0.5%)	referent
COPD/pneumonia-related mortality	New SSRI or SNRI users	118(0.8%)	0.75 (0.59-0.94), 0.01
	New benzodiazepine users	156(1.0%)	referent
All-cause mortality	New SSRI or SNRI users	798(5.3%)	0.75 (0.68-0.82), <0.0001
	New benzodiazepine users	1054(7.0%)	referent

Table 4. Hazard ratios and confidence intervals for outcomes in the community-dwelling propensity matched cohort, where the control group was tricyclic antidepressant drug users

Outcomes	Status of SSRI/SNRI use	Number of events (%)	HR (95% CI, p-value)
Outpatient respiratory exacerbation	New SSRI or SNRI users	2121 (8.4%)	0.93 (0.86-1.01, 0.10)
	New tricyclic users	1047 (9.0%)	referent
ER visit for COPD or pneumonia	New SSRI or SNRI users	793 (3.1%)	1.00 (0.87-1.16, 0.99)
	New tricyclic users	366 (3.1%)	referent
Hospital admissions COPD or pneumonia	New SSRI or SNRI users	965 (3.8%)	1.18 (1.03-1.37, 0.02)
	New tricyclic users	378 (3.2%)	referent
ICU admission during a hospitalization for COPD or pneumonia	New SSRI or SNRI users	140 (0.6%)	1.22 (0.84-1.77, 0.30)
	New tricyclic users	53 (0.5%)	referent
COPD or pneumonia-related mortality	New SSRI or SNRI users	186 (0.7%)	1.57 (1.07-2.29, 0.02)
	New tricyclic users	55 (0.5%)	referent
All-cause mortality	New SSRI or SNRI users	1274 (5.1%)	1.39 (1.22-1.59, <0.001)
	New tricyclic users	426 (3.7%)	referent

Section 4: Results of long-term care home resident cohort analysis

Overall cohort results

Between April 1, 2008 and December 31, 2013, 13,107 long-term care home residents with COPD were identified and 6231 (47.5%) of them were new SSRI/SNRI users (Figure 1 in this section). After propensity score matching, 5053 new users were matched to an equivalent number of controls. No matched control was found for 1178 (18.9%) of new SSRI/SNRI users. New users and controls were well-balanced on baseline characteristics, with standardized differences being below 10% for all variables (Table 1 in this section).

Compared to controls, new SSRI/SNRI users had significantly higher rates of COPD or pneumonia-related mortality (ARD 0.09%; HR 1.42, 95% CI 1.13-1.80; NNH 111) and all-cause mortality (ARD 4.5%; HR 1.32, 95% CI 1.19-1.46; NNH 22), but decreased significantly decreased rate of outpatient exacerbation (HR 0.84; 95% CI 0.72-0.97) (Table 2 in this section). No other significant associations were observed. These results are similar to the community-dwelling cohort, with the exception that in the community-dwelling cohort significantly increased rates of hospital admission for COPD or pneumonia and ER visits for COPD or pneumonia were also found. The aforementioned differences between the two cohorts may be explained by the fact that far fewer long-term care home residents were available for analysis (13,107 long-term care residents versus 118,611 community-dwelling individuals) and more SSRI/SNRI users went entirely unmatched in the long-term care home resident cohort (18.9% in long-term care versus 4.9% in the community). In addition, patterns of hospital referral may be different for long-term care residents as compared to community-dwelling older adults. For example, long-term care residents with COPD may receive care on-site within the nursing home

setting for COPD or pneumonia, thereby potentially resulting in fewer ER visits and hospitalizations for these conditions than would be seen with community-dwelling individuals with similar conditions. This difference helps to justify the approach used in this study, where community-dwelling older adults and long-term care residents were examined separately.

Sensitivity analyses

By COPD exacerbation frequency. In the subgroup of individuals with no exacerbation in the year prior to index, new versus non-users had significantly decreased rates of outpatient exacerbations (HR 0.75; 95% 0.58-0.98) (Table 3 in this section). In the subgroup of individuals with >=1 exacerbation requiring hospitalization in the year prior to index, significantly lower rates of ER visits for COPD or pneumonia was found among new versus non-users (HR 0.61; 95% 0.38-0.99). A significantly increased rate of COPD or pneumonia-related mortality was observed among new versus non-users in the subgroup with >=1 outpatient respiratory exacerbation in the year prior to index (HR 2.82; 95% CI 1.18-6.77). There were significantly increased rates of all-cause mortality among new versus non-users across all COPD exacerbation frequency subgroups (no exacerbations in the year prior to index: HR 1.31; 95% CI 1.14-1.50; >=1 outpatient respiratory exacerbation in the year prior to index: HR 1.96; 95% CI 1.35-2.86; >=1 exacerbation requiring hospitalization in the year prior to index: HR 1.23; 95% CI 1.03-1.46). No other associations were statistically significant. A fairly similar pattern of results was seen in the community-dwelling cohort.

By previously diagnosed psychiatric disease. In the subgroup of individuals without pre-existing psychiatric disease, there were significantly increased rates of COPD or pneumonia-

related mortality (HR 1.68; 95% CI 1.17-2.42) and all-cause mortality (HR 1.45; 95% CI 1.24-1.71) among new users compared to controls (Table 4 in this section). In the subgroup of individuals with pre-existing psychiatric disease, new users compared to controls had significantly lower rate of outpatient exacerbation (HR 0.80; 95% CI 0.67-0.97), but significantly higher all-cause mortality rate (HR 1.23; 95% CI 1.08-1.41). There were no other significant associations observed. While increased mortality risk associated with SSRI/SNRI drug use was found among individuals without pre-existing psychiatric disease in both the community-dwelling and long-term care home resident cohorts, this finding was observed to extend to those with pre-existing psychiatric disease among long-term care home residents.

By SSRI versus SNRI drug class. Individuals receiving a new SSRI drug versus controls had significantly decreased rate of outpatient exacerbation (HR 0.84; 95% CI 0.71-0.98) and significantly increased rates of COPD or pneumonia-related mortality (HR 1.42; 95% CI 1.11-1.81) and all-cause mortality (HR 1.29; 95% CI 1.15-1.44) (Table 5 in this section). Compared to controls, individuals receiving a new SNRI drug had significantly higher rate of all-cause mortality (HR 1.56; 95% CI 1.18-2.08). No other associations were statistically significant. Similar to community-dwelling individuals, new SSRI use was found to be associated with increased risk of death among long-term care home residents, but unlike the community-dwelling cohort, increased mortality risk additionally extended to new SNRI use in the long-term care home resident group.

By citalopram daily dose category. Compared to controls, individuals receiving lower daily doses of citalopram had significantly decreased rate of outpatient exacerbation (HR 0.68;

95% CI 0.52-0.88), but significantly increased rate of all-cause mortality (HR 1.22; 95% CI 1.02-1.46) (Table 6 in this section). Individuals receiving higher daily doses of citalopram versus controls also had significantly increased rate of all-cause mortality (HR 1.34; 95% CI 104-1.73). No other associations were statistically significant. Similar to the community-dwelling group, increased all-cause mortality was found to extend to lower dose citalopram users in the long-term care home resident cohort, but in addition, a dose-response relationship between citalopram and mortality was observed in the long-term care home group. Although there were a greater number of significantly increased adverse outcomes in association with lower dose citalopram use in the community-dwelling group, the smaller overall size of the long-term care home resident group, and the fact that more exposed individuals went unmatched in the latter cohort, may have contributed to an inability to detect more significant findings.

With new benzodiazepine users serving as controls. Compared to new benzodiazepine users, new SSRI/SNRI users had significantly decreased rates of COPD or pneumonia-related mortality (HR 0.61; 95% CI 0.48-0.78) and all-cause mortality (HR 0.63; 95% CI 0.57-0.71) (Table 7 in this section). No other outcomes were found to be statistically significant. A similar pattern of results was observed in the community-dwelling cohort.

With new tricyclic antidepressant users serving as controls. There were no significant associations observed between incident SSRI/SNRI drug use and our adverse respiratory outcomes, when new tricyclic antidepressant users formed the control group (Table 8 in this section). This sensitivity analysis may have been under-powered to detect potentially true

significant differences, given that in the relatively larger community-dwelling group significant differences were seen between exposed and control individuals.

Figure 1. Flow diagram outlining exposed and control group identification in the long-term care home resident cohort

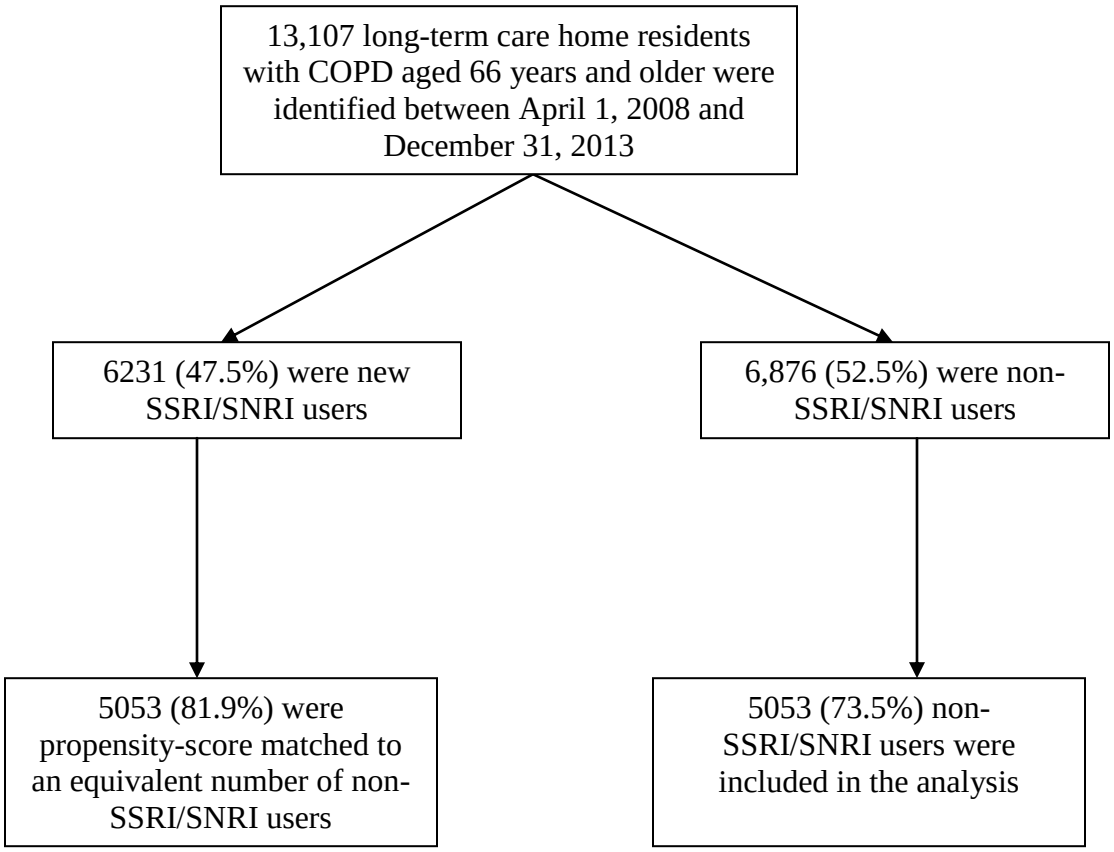

Table 1. Baseline characteristics of long-term care home resident cohort, before and after propensity score matching (full list of covariates included in the propensity score model)

	Before propensity score matching			After propensity score matching		
	New SSRI/SNRI users	**Non-SSRI/ SNRI users**	**Standardized difference[a]**	**New SSRI/SNRI users**	**Non-SSRI/ SNRI users**	**Standardized difference[a]**
	N=6,231	N=6,876		N=5,053	N=5,053	
Age (mean + SD)	83.8 ± 7.1	85.4 ± 7.5	0.23	84.5 ± 6.9	84.6 ± 7.6	0.01
% female	58.4%	59.8%	0.03	59.3%	59.3%	0.0008
Low income as per ODB flag (%)	37.6%	40.2%	0.05	38.7%	39.1%	0.009
Income quintile (%)						
1 (lowest)	25.1%	26.1%	0.02	25.9%	26.1%	0.005
2	20.4%	19.4%	0.02	19.8%	20.6%	0.02
3	20.3%	19.6%	0.02	19.8%	19.5%	0.008
4	18.1%	17.7%	0.01	18.0%	17.8%	0.005
5 (highest)	15.3%	16.3%	0.03	15.8%	15.3%	0.01
Missing data	0.8%	0.9%	0.01	0.8%	0.7%	0.009
% rural setting	18.7%	15.8%	0.08	17.4%	17.4%	0.0005
COPD exacerbation frequency in the past year (%)						
0	64.9%	63.1%	0.04	66.0%	66.0%	0
>=1 outpatient exacerbation	7.9%	11.0%	0.11	8.6%	8.6%	0
>=1 exacerbation requiring hospital presentation	27.2%	25.9%	0.03	25.5%	25.5%	0
COPD exacerbation in the past 30 days (%)	5.7%	9.2%	0.13	6.5%	6.2%	0.01
Duration of COPD year prior (%)						
< 2 years	20.6%	30.3%	0.22	24.2%	23.6%	0.01
2-5 years	17.2%	17.1%	0.003	17.5%	17.6%	0.001
> 5 years	62.2%	52.7%	0.19	58.3%	58.9%	0.01

Table 1 continued from previous page						
	Before propensity score matching			**After propensity score matching**		
	New SSRI/SNRI users	**Non-SSRI/ SNRI users**	**Standardized difference[a]**	**New SSRI/SNRI users**	**Non-SSRI/ SNRI users**	**Standardized difference[a]**
	N=6,231	N=6,876		N=5,053	N=5,053	
Respiratory medications in the past 6 months (%)						
Short/long-acting beta agonists	37.3%	39.9%	0.05	37.8%	37.9%	0.002
Short/long-acting anticholinergics	38.4%	41.0%	0.05	39.5%	39.8%	0.006
Inhaled corticosteroids	13.1%	16.1%	0.08	14.2%	14.3%	0.003
Combination inhaled corticosteroid-long acting beta agonist inhalers	27.3%	26.1%	0.03	26.7%	26.6%	0.002
Oral corticosteroids	13.1%	12.8%	0.009	12.5%	12.3%	0.008
Theophylline	1.6%	1.3%	0.02	1.6%	1.4%	0.02
Respiratory antibiotics	48.7%	55.5%	0.14	51.7%	52.0%	0.006
Total number of outpatient visits in the past 12 months (mean + SD)	18.9 ± 16.7	18.7 ± 14.4	0.01	18.5 ± 15.9	18.6 ± 14.1	0.005
Total number of hospitalizations in the past 12 months (mean + SD)	0.93 ± 1.17	0.78 ± 1.09	0.1358	0.84 ± 1.11	0.83 ± 1.14	0.012
Any ICU admission in the past 12 months (%)	602 (9.7%)	494 (7.2%)	0.0893	406 (8.0%)	414 (8.2%)	0.0058
Any surgery in the past 12 months (%)	700 (11.2%)	584 (8.5%)	0.092	481 (9.5%)	485 (9.6%)	0.0027
Johns Hopkins Adjusted Clinical Group[b] (%)						
Bottom tertile	29.3%	40.3%	0.23	34.4%	35.0%	0.01
Middle tertile	23.2%	21.7%	0.04	23.4%	22.9%	0.01
Top tertile	47.5%	38.0%	0.19	42.2%	42.1%	0.003
Non-COPD pulmonary disease[c] (%)	42.5%	38.0%	0.09	39.8%	39.4%	0.009
Ischemic heart disease[c] (%)	39.8%	34.8%	0.10	37.7%	37.7%	0.0004

Table 1 continued from previous page						
	Before propensity score matching			After propensity score matching		
	New SSRI/SNRI users	Non-SSRI/ SNRI users	Standardized difference[a]	New SSRI/SNRI users	Non-SSRI/ SNRI users	Standardized difference[a]
	N=6,231	N=6,876		N=5,053	N=5,053	
Congestive heart failure[c] (%)	46.5%	47.1%	0.01	46.9%	47.1%	0.004
ER visit/hospitalization for ischemic heart disease or congestive heart failure in the year prior (%)	23.2%	20.0%	0.08	21.4%	21.2%	0.004
Hypertension[c] (%)	84.9%	81.7%	0.09	83.7%	83.6%	0.003
Atherosclerosis[c] (%)	8.4%	8.4%	0.0005	8.3%	8.3%	0.0007
Diabetes[c] (%)	38.7%	36.7%	0.04	37.9%	37.9%	0.0004
Previous stroke and cerebrovascular disease[c] (%)	31.3%	29.1%	0.045	30.2%	30.5%	0.007
Cancer[c] (%)	22.5%	21.8%	0.02	22.2%	22.0%	0.005
Musculoskeletal or connective tissue disease[c] (%)	92.8%	91.2%	0.06	92.1%	92.1%	0
Osteoporosis[c] (%)	16.8%	16.6%	0.006	16.6%	16.5%	0.002
Psychotic psychiatric disease[c,e] (%)	21.9%	19.8%	0.05	21.1%	21.4%	0.007
Non-psychotic psychiatric disease[c,f] (%)	61.6%	49.7%	0.24	57.0%	56.8%	0.004
Sleep disorder[c] (%)	53.2%	48.4%	0.10	50.4%	50.8%	0.008
Total number of non-SSRI/SNRI drugs received in the past year (mean + SD)	15.8 ± 8.0	15.9 ± 6.9	0.01	15.9 ± 7.8	15.9 ± 7.0	0.001

Table 1 continued from previous page

	Before propensity score matching			After propensity score matching		
	New SSRI/SNRI users	**Non-SSRI/ SNRI users**	**Standardized difference[a]**	**New SSRI/SNRI users**	**Non-SSRI/ SNRI users**	**Standardized difference[a]**
	N=6,231	N=6,876		N=5,053	N=5,053	
Benzodiazepine in the past 6 months (%)	32.5%	28.9%	0.08	31.2%	31.7%	0.01
Oral/transdermal opioid in the past 6 months (%)	34.2%	29.8%	0.09	32.7%	32.6%)	0.003
Smoking cessation drug[g] in the past 12 months (%)	1.6%	1.1%	0.04	1.3%)	1.3%)	0.007
Spirometry in the past 12 months (%)	8.0%	5.1%	0.12	6.1%	6.0%)	0.003
% cohort entry in flu season[h]	39.1%	33.8%	0.11	36.5%	36.3%	0.005

ER = emergency room; ODB = Ontario Drug Benefit; SD = standard deviation

[a]Standardized differences of > 0.10 are thought to indicate potentially meaningful differences.

[b]This is a measure of patient morbidity burden, using hospitalization and ambulatory visit data based on a 2-year look-back from the index date. The Johns Hopkins ACG(r) System Ver XX.

[c]Presence of comorbidities was based on 5-year look-back from the index date.

[e]Includes schizophrenia, bipolar disorder and paranoid states.

[f]Includes depression disorders, anxiety disorders, phobias, stress disorders, dissociative and somatization disorders, eating disorders, personality disorders, mental and behavioural disorders due to substance abuse, and tic disorders.

[g]Includes Wellbutrin and Varenicline.

[h]Defined as November 1 to March 31.

Table 2. Hazard ratios and confidence intervals for outcomes in the propensity score matched long term care home resident cohort

Outcomes	Status of SSRI/SNRI use	Number of events (%)	HR (95% CI, p-value)
Outpatient respiratory exacerbation	New SSRI or SNRI users	299(5.9%)	0.84 (0.72-0.97), 0.02
	Non- SSRI or SNRI users	355(7.0%)	Referent
ER visit for COPD or pneumonia	New SSRI or SNRI users	87(1.7%)	0.99 (0.74-1.33), 0.94
	Non- SSRI or SNRI users	88(1.7%)	Referent
Hospital admissions COPD or pneumonia	New SSRI or SNRI users	218(4.3%)	1.05 (0.88-1.27), 0.56
	Non- SSRI or SNRI users	207(4.1%)	Referent
ICU admission during a hospitalization for COPD or pneumonia	New SSRI or SNRI users	20(0.4%)	1.05 (0.56-1.98), 0.87
	Non- SSRI or SNRI users	19(0.4%)	Referent
COPD/pneumonia-related mortality	New SSRI or SNRI users	169(3.3%)	1.42 (1.13-1.80), 0.003
	Non- SSRI or SNRI users	122(2.4%)	Referent
All-cause mortality	New SSRI or SNRI users	808(16.0%)	1.32 (1.19-1.46), <0.0001
	Non- SSRI or SNRI users	631(12.5%)	Referent

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ER = emergency room; HR = hazard ratio; ICU = intensive care unit

Table 3. Hazard ratios and confidence intervals for outcomes in the propensity score matched long term care home resident cohort, stratified by COPD exacerbation frequency

COPD exacerbation frequency status	SSRI/ SNRI status	Outpatient exacerbation		ER visit for COPD or pneumonia		Hospital admission COPD or pneumonia		ICU admission during a hospitalization for COPD or pneumonia		COPD or pneumonia-related mortality		All-cause mortality	
		N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value
0 exacerbation in the year prior to index	New users	100 (3.0%)	0.75 (0.58-0.98), 0.03	48 (1.4%)	1.23 (0.82-1.87), 0.32	88 (2.6%)	1.13 (0.84-1.53), 0.43	6 (0.2%)	1.00 (0.32-3.10), 1.00	70 (2.1%)	1.43 (0.99-2.06), 0.05	462 (13.9%)	1.31 (1.14-1.50), 0.0001
	Non-users	132 (4.0%)		39 (1.2%)		78 (2.3%)		6 (0.2%)		50 (1.5%)		361 (10.8%)	
>=1 outpatient respiratory exacerbation in the year prior to index	New users	72 (16.6%)	0.91 (0.67-1.23), 0.53	12 (2.8%)	2.41 (0.84-6.90), 0.10	22 (5.1%)	1.38 (0.74-2.58), 0.31	<6[a]	1.00 (0.14-7.12), 1.00	19 (4.4%)	2.82 (1.18-6.77), 0.02	73 (16.8%)	1.96 (1.35-2.86), 0.0005
	Non-users	78 (18.0%)		<6[a]		16 (3.7%)		<6[a]		7 (1.6%)		39 (9.0%)	
>=1 exacerbation requiring presentation to hospital in the year prior to index	New users	127 (9.9%)	0.87 (0.69-1.10), 0.24	27 (2.1%)	0.61 (0.38-0.99), 0.05	108 (8.4%)	0.96 (0.73-1.24), 0.74	12 (0.9%)	1.09 (0.48-2.49), 0.83	80 (6.2%)	1.28 (0.92-1.77), 0.14	273 (21.2%)	1.23 (1.03-1.46), 0.02
	Non-users	145 (11.3%)		44 (3.4%)		113 (8.8%)		11 (0.9%)		65 (5.1%)		231 (18.0%)	

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ER = emergency room; HR = hazard ratio; ICU = intensive care unit; N = number

[a]Data are not presented, according to Institute of Clinical Evaluative Sciences reporting rules, because of small cell size

Table 4. Hazard ratios and confidence intervals for outcomes in the propensity score matched long term care home resident cohort, stratified by presence of pre-existing psychiatric disease

Pre-existing psychiatric disease[a] status	SSRI/ SNRI status	Outpatient exacerbation		ER visit for COPD or pneumonia		Hospital admission COPD or pneumonia		ICU admission during a hospitalization for COPD or pneumonia		COPD or pneumonia-related mortality		All-cause mortality	
		N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value		N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)
No known pre-existing psychiatric disease	New users	105 (5.7%)	0.90 (0.70-1.16), 0.41	27 (1.5%)	0.77 (0.46-1.28), 0.31	77 (4.1%)	1.12 (0.82-1.53), 0.49	10 (0.5%)	1.67 (0.61-4.60), 0.32	76 (4.1%)	1.68 (1.17-2.42), 0.005	338(18.2%)	1.45 (1.24-1.71), <0.0001
	Non-users	116 (6.2%)		35 (1.9%)		69 (3.7%)		6 (0.3%)		47 (2.5%)		242(13.0%)	
Known pre-existing psychiatric disease	New users	194 (6.1%)	0.80 (0.67-0.97), 0.020	60 (1.9%)	1.13 (0.79-1.64), 0.50	141 (4.4%)	1.02 (0.81-1.29), 0.84	10 (0.3%)	0.77 (0.34-1.76), 0.53	93 (2.9%)	1.27 (0.94-1.71), 0.13	470(14.7%)	1.23 (1.08-1.41), 0.002
	Non-users	239 (7.5%)		53 (1.7%)		138 (4.3%)		13 (0.4%)		75 (2.3%)		389 (12.2%)	

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ER = emergency room; HR = hazard ratio; ICU = intensive care unit; N = number

[a] An individual was considered to have psychiatric disease if any one of the following conditions were present: schizophrenia; bipolar disorder; paranoid states; depression disorders; anxiety disorders; phobias; stress disorders; dissociative and somatization disorders; eating disorders; personality disorders; mental and behavioural disorders due to substance abuse; and, tic disorders.

Table 5. Hazard ratios and confidence intervals for outcomes in the long term care home resident propensity matched cohort, distinguishing by SSRI/SNRI drug class received

SSRI/SNRI drug class received	SSRI/ SNRI status	Outpatient exacerbation		ER visit for COPD or pneumonia		Hospital admission COPD or pneumonia		ICU admission during a hospitalization for COPD or pneumonia		COPD or pneumonia-related mortality		All-cause mortality	
		N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value
SSRI drugs	New users	266 (6.1%)	0.84 (0.71-0.98), 0.03	81 (1.8%)	1.03 (0.75-1.40), 0.87	185 (4.2%)	1.02 (0.84-1.25), 0.83	17 (0.4%)	1.13 (0.57-2.27), 0.72	152 (3.5%)	1.42 (1.11-1.81), 0.005	698 (15.9%)	1.29 (1.15-1.44), <0.0001
	Non-users	316 (7.2%)		79 (1.8%)		181 (4.1%)		15 (0.3%)		110 (2.5%)		557 (12.7%)	
SNRI drugs	New users	33 (5.0%)	0.84 (0.53-1.33), 0.45	6 (0.9%)	0.66 (0.24-1.88), 0.44	33 (5.0%)	1.28 (0.78-2.10), 0.33	<6[a]	0.75 (0.17-3.37), 0.71	18 (2.7%)	1.57 (0.75-3.27), 0.23	111 (16.8%)	1.56 (1.18-2.08), 0.002
	Non-users	39 (5.9%)		9 (1.4%)		26 (3.9%)		<6[a]		12 (1.8%)		74 (11.2%)	

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ER = emergency room; HR = hazard ratio; ICU = intensive care unit; N = number

[a]Data are not presented, according to Institute of Clinical Evaluative Sciences reporting rules, because of small cell size

Table 6. Hazard ratios and confidence intervals for outcomes in the long term care home resident propensity matched cohort, distinguishing by citalopram daily dose

Citalo-pram daily dose	SSRI/ SNRI status	Outpatient exacerbation		ER visit for COPD or pneumonia		Hospital admission COPD or pneumonia		ICU admission during a hospitalization for COPD or pneumonia		COPD or pneumonia-related mortality		All-cause mortality	
		N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value	N (%)	HR (95% CI), p-value
Lower dose (< 20 mg/day)	New users	89 (5.7%)	0.68 (0.52-0.88), 0.004	33 (2.1%)	1.38 (0.82-2.32), 0.23	67 (4.3%)	1.23 (0.87-1.74), 0.25	6 (0.4%)	1.00 (0.32-3.11), 1.00	49 (3.1%)	1.39 (0.90-2.15), 0.14	245 (15.6%)	1.22 (1.02-1.46), 0.03
	Non-users	130 (8.3%)		24 (1.5%)		55 (3.5%)		6 (0.4%)		36 (2.3%)		205 (13.1%)	
Higher dose (>=20 mg/day)	New users	46 (5.3%)	0.86 (0.58-1.27), 0.45	11 (1.3%)	0.73 (0.35-1.55), 0.42	34 (3.9%)	0.89 (0.56-1.42), 0.62	<6[a]	3.00 (0.31-28.90), 0.34	23 (2.7%)	1.13 (0.62-2.05), 0.70	136 (15.7%)	1.34 (1.04-1.73), 0.02
	Non-users	53 (6.1%)		15 (1.7%)		38 (4.4%)		<6[a]		21 (2.4%)		104 (12.0%)	

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ER = emergency room; HR = hazard ratio; ICU = intensive care unit; N = number

[a]Data are not presented, according to Institute of Clinical Evaluative Sciences reporting rules, because of small cell size

Table 7. Hazard ratios and confidence intervals for outcomes in the long term care home resident propensity matched cohort, where the control group was new benzodiazepine drug users

Outcomes	SSRI/SNRI use status	Number of events (%)	HR (95% CI), p-value
Outpatient respiratory exacerbation	New SSRI/SNRI users	188 (5.7%)	0.84 (0.70-1.02), 0.08
	New benzodiazepine users	221 (6.7%)	referent
ER visit for COPD or pneumonia	New SSRI/SNRI users	63(1.9%)	0.95 (0.67-1.35), 0.79
	New benzodiazepine users	66 (2.0%)	referent
Hospital admissions COPD or pneumonia	New SSRI/SNRI users	153 (4.6%)	1.06 (0.85-1.33), 0.61
	New benzodiazepine users	144 (4.4%)	Referent
ICU admission during a hospitalization for COPD or pneumonia	New SSRI/SNRI users	15 (0.5%)	0.75 (0.38-1.47), 0.40
	New benzodiazepine users	20 (0.6%)	referent
COPD or pneumonia-related mortality	New SSRI/SNRI users	102 (3.1%)	0.61 (0.48-0.78), 0.0001
	New benzodiazepine users	156 (4.7%)	referent
All-cause mortality	New SSRI/SNRI users	534 (16.2%)	0.63 (0.57-0.71), <0.0001
	New benzodiazepine users	783 (23.8%)	referent

Table 8. Hazard ratios and confidence intervals for outcomes in the long-term care home resident propensity matched cohort, where the control group was tricyclic antidepressant drug users

Outcomes	Status of SSRI/SNRI use	Number of events (%)	HR (95% CI, p-value)
Outpatient respiratory exacerbation	New SSRI or SNRI users	333 (5.9%)	0.79 (0.55-1.14, 0.20)
	New tricyclic users	48 (7.4%)	referent
ER visis for COPD or pneumonia	New SSRI or SNRI users	98 (1.7%)	1.29 (0.61-2.75, 0.50)
	New tricyclic users	9 (1.3%)	referent
Hospital admissions COPD or pneumonia	New SSRI or SNRI users	258 (4.5%)	0.87 (0.59-1.29, 0.48)
	New tricyclic users	34 (5.2%)	referent
ICU admission during a hospitalization for COPD or pneumonia	New SSRI or SNRI users	30 (0.5%)	0.80 (0.34-1.90, 0.61)
	New tricyclic users	<6[a]	referent
COPD or pneumonia-related mortality	New SSRI or SNRI users	186 (3.3%)	1.07 (0.63-1.81, 0.81)
	New tricyclic users	20 (3.1%)	referent
All-cause mortality	New SSRI or SNRI users	890 (15.7%)	1.04 (0.82-1.32, 0.74)
	New tricyclic users	97 (15.0%)	referent

[a] Data are not presented, according to Institute of Clinical Evaluative Sciences reporting rules, because of small cell size