

Table E1. Age-adjusted incidence rate ratio of pneumonia (first event) in exposure periods after antidepressant prescription relative to unexposed periods in patients with COPD, calculated by case series analytical technique, UK, 2004-2015

Antidepressants	No. of exposed cases with Pneumonia	Day 1-30 IRR (95% CI)	Day 31-60 IRR (95% CI)	Day 61-90 IRR (95% CI)	Day 1-90 IRR (95% CI)	Remainder period IRR (95% CI)	90 days washout IRR (95% CI)
Collective	1,969	1.54	1.57	1.59	1.51	2.15	0.92
Antidepressants		(1.13 to 2.10)	(1.18 to 2.08)	(1.08 to 2.34)	(1.45 to 2.17)	(1.86 to 2.48)	(0.62 to 1.38)
SSRI or NRI	1,218	1.69	1.55	2.51	1.79	1.91	1.02
		(1.21 to 2.35)	(1.15 to 2.10)	(1.80 to 3.15)	(1.46 to 2.18)	(1.64 to 2.23)	(0.68 to 1.54)
SSRI	1,143	1.71	1.45	2.60	1.70	1.89	0.95
		(1.21 to 2.41)	(1.05 to 2.01)	(1.85 to 3.66)	(1.38 to 2.08)	(1.61 to 2.22)	(0.61 to 1.47)
SNRI	168	1.99	1.42	1.47	1.59	2.20	2.23
		(0.85 to 4.69)	(0.60 to 2.38)	(0.46 to 4.66)	(0.90 to 2.80)	(1.35 to 3.02)	(0.103 to 4.84)
TCA	1,318	1.61	1.75	1.28	1.55	1.77	1.28
		(1.17 to 2.21)	(1.29 to 2.38)	(0.83 to 1.98)	(1.26 to 1.90)	(1.51 to 2.08)	(0.90 to 1.81)
MAOI	50	1.02	1.22	—	0.95	2.03	1.06
		(0.09 to 11.2)	(0.10 to 12.3)		(0.18 to 4.81)	(0.66 to 6.21)	(0.14 to 8.18)

The “Collective Antidepressants” does not equate to the total of all individual class as some subjects received more than one antidepressant in each class

Exposure time periods:

- 1- Day 1-30: A 30-day risk period starting from the day after the date of prescription.
- 2- Day 31-60: A 30-day risk period starting from day 31 after the date of prescription.
- 3- Day 61-90: A 30-day risk period starting from day 61 after the date of prescription.
- 4- Day 1-90: A 90-day risk period accounts for the entire risk window (day 1 to 90).
- 5- Remainder period: A period starts 90 days after the date of the prescription until the end of the course (from day 91 after date of prescription until the end of the course).
- 6- 90 days washout: A 90-day period starting the day after the end of the course and continuing for 90 days (day 1 after the end of the course until day 90 after the end of the course). Abbreviations: SSRI: Selective Serotonin Reuptake Inhibitor; SNRI: serotonin-norepinephrine reuptake Inhibitor; TCA: Tricyclic antidepressants; MAOI: Monoamine oxidase inhibitors.

Table E2. Age-adjusted incidence rate ratio of pneumonia (excluding cases who died within 6 months following the date of pneumonia diagnosis) in exposure periods after antidepressant prescription relative to unexposed periods in patients with COPD, calculated by case series analytical technique, UK, 2004-2015

Antidepressants	No. of exposed cases with Pneumonia	Day 1-30 IRR (95% CI)	Day 31-60 IRR (95% CI)	Day 61-90 IRR (95% CI)	Day 1-90 IRR (95% CI)	Remainder period IRR (95% CI)	90 days washout IRR (95% CI)
Collective	1,674	1.33 (1.12 to 1.66)	1.64 (1.30 to 2.07)	1.44 (1.04 to 2.02)	1.48 (1.26 to 1.75)	1.56 (1.37 to 1.77)	0.85 (0.59 to 1.23)
SSRI or SNRI	1,048	1.32 (0.92 to 1.89)	1.44 (1.05 to 1.97)	2.03 (1.41 to 2.91)	1.50 (1.22 to 1.84)	1.51 (1.28 to 1.78)	0.86 (0.55 to 1.34)
SSRI	978	1.26 (0.86 to 1.85)	1.41 (1.02 to 1.95)	2.15 (1.49 to 3.1)	1.55 (1.26 to 1.91)	1.48 (1.26 to 1.75)	0.83 (0.52 to 1.33)
SNRI	157	0.89 (0.30 to 2.70)	1.15 (0.46 to 2.84)	1.72 (0.63 to 4.67)	1.17 (0.64 to 2.15)	1.81 (1.22 to 2.70)	2.03 (0.93 to 4.39)
TCA	1,121	1.24 (0.88 to 1.74)	1.71 (1.27 to 2.30)	1.21 (0.77 to 1.88)	1.42 (1.15 to 1.74)	1.56 (1.32 to 1.83)	1.04 (0.71 to 1.54)
MAOI	45	0.83 (0.08 to 7.86)	0.91 (0.10 to 8.46)	—	0.62 (0.13 to 3.02)	1.70 (0.58 to 4.94)	1.47 (0.36 to 6.14)

The "Collective Antidepressants" does not equate to the total of all individual class as some subjects received more than one antidepressant in each class

Exposure time periods:

- 1- Day 1-30: A 30-day risk period starting from the day after the date of prescription.
- 2- Day 31-60: A 30-day risk period starting from day 31 after the date of prescription.
- 3- Day 61-90: A 30-day risk period starting from day 61 after the date of prescription.
- 4- Day 1-90: A 90-day risk period accounts for the entire risk window (day 1 to 90).
- 5- Remainder period: A period starts 90 days after the date of the prescription until the end of the course (from day 91 after date of prescription until the end of the course)
- 6- 90 days washout: A 90-day period starting the day after the end of the course and continuing for 90 days (day 1 after the end of the course until day 90 after the end of the course). Abbreviations: SSRI: Selective Serotonin Reuptake Inhibitor; SNRI: serotonin-norepinephrine reuptake Inhibitor; TCA: Tricyclic antidepressants; MAOI: Monoamine oxidase inhibitors.

Table E3. Age-adjusted incidence rate ratio of pneumonia (excluding cases who died within 12 months following the date of pneumonia diagnosis) in exposure periods after antidepressant prescription relative to unexposed periods in patients with COPD, calculated by case series analytical technique, UK, 2004-2015

Antidepressants	No. of exposed cases with Pneumonia	Day 1-30 IRR (95% CI)	Day 31-60 IRR (95% CI)	Day 61-90 IRR (95% CI)	Day 1-90 IRR (95% CI)	Remainder period IRR (95% CI)	90 days washout IRR (95% CI)
Collective	1,581	1.32 (1.02 to 1.75)	1.51 (1.18 to 1.92)	1.46 (1.04 to 2.05)	1.43 (1.21 to 1.70)	1.48 (1.30 to 1.68)	0.79 (0.53 to 1.17)
Antidepressants							
SSRI or SNRI	989	1.33 (0.92 to 1.91)	1.38 (1.01 to 1.89)	1.97 (1.36 to 2.87)	1.48 (1.19 to 1.83)	1.42 (1.20 to 1.68)	0.87 (0.57 to 1.39)
SSRI	922	1.24 (0.85 to 1.84)	1.23 (0.87 to 1.74)	2.02 (1.38 to 2.69)	1.51 (1.22 to 1.86)	1.34 (1.12 to 1.60)	0.86 (0.54 to 1.38)
SNRI	153	0.91 (0.30 to 2.76)	1.16 (0.47 to 2.90)	1.77 (0.65 to 4.82)	1.19 (0.65 to 2.19)	1.75 (1.61 to 2.63)	2.09 (0.97 to 4.54)
TCA	1,065	1.25 (0.88 to 1.76)	1.58 (1.16 to 2.15)	1.19 (0.75 to 1.88)	1.40 (1.13 to 1.72)	1.50 (1.27 to 1.78)	0.95 (0.62 to 1.44)
MAOI	44	0.85 (0.09 to 8.05)	0.93 (0.10 to 8.64)	—	0.64 (0.13 to 3.10)	1.76 (0.60 to 5.16)	1.50 (0.36 to 6.32)

The “Collective Antidepressants” does not equate to the total of all individual class as some subjects received more than one antidepressant in each class

Exposure time periods:

- 1- Day 1-30: A 30-day risk period starting from the day after the date of prescription.
- 2- Day 31-60: A 30-day risk period starting from day 31 after the date of prescription.
- 3- Day 61-90: A 30-day risk period starting from day 61 after the date of prescription.
- 4- Day 1-90: A 90-day risk period accounts for the entire risk window (day 1 to 90).
- 5- Remainder period: A period starts 90 days after the date of the prescription until the end of the course (from day 91 after date of prescription until the end of the course)
- 6- 90 days washout: A 90-day period starting the day after the end of the course and continuing for 90 days (day 1 after the end of the course until day 90 after the end of the course). Abbreviations: SSRI: Selective Serotonin Reuptake Inhibitor; SNRI: serotonin-norepinephrine reuptake Inhibitor; TCA: Tricyclic antidepressants; MAOI: Monoamine oxidase inhibitors.

Table E4. Age-adjusted incidence rate ratio of COPD exacerbation (first event) in exposure periods after antidepressant prescription relative to unexposed periods in patients with COPD, calculated by case series analytical technique, UK, 2004-2015

Antidepressant	No. of exposed cases with exacerbation	Day 1-30 IRR (95% CI)	Day 31-60 IRR (95% CI)	Day 61-90 IRR (95% CI)	Day 1-90 IRR (95% CI)	Remainder period IRR (95% CI)	90 days washout IRR (95% CI)
Collective	18483	1.41 (1.30 to 1.52)	1.21 (1.12 to 1.31)	1.73 (1.59 to 1.89)	1.41 (1.34 to 1.49)	1.34 (1.28 to 1.39)	0.97 (0.85 to 1.10)
Antidepressants							
SSRI or SNRI	11,770	1.48 (1.34 to 1.64)	1.19 (1.08 to 1.32)	1.73 (1.54 to 1.93)	1.43 (1.34 to 1.53)	1.39 (1.32 to 1.45)	1.12 (0.98 to 1.27)
SSRI	20,885	1.45 (1.30 to 1.61)	1.18 (1.06 to 1.31)	1.62 (1.44 to 1.83)	1.39 (1.30 to 1.49)	1.37 (1.30 to 1.44)	0.97 (0.85 to 1.10)
SNRI	4,128	1.29 (0.97 to 1.72)	1.56 (1.17 to 2.07)	2.24 (1.71 to 2.92)	1.64 (1.38 to 1.95)	1.32 (1.16 to 1.50)	1.26 (0.88 to 1.78)
TCA	23,786	1.36 (1.22 to 1.51)	1.22 (1.10 to 1.35)	1.70 (1.52 to 1.91)	1.23 (1.16 to 1.30)	1.23 (1.17 to 1.31)	0.98 (0.86 to 1.07)
MAOI	416	0.98 (0.48 to 2.00)	1.18 (0.67 to 2.09)	1.62 (0.83 to 13.1)	1.23 (0.83 to 1.81)	1.15 (0.78 to 1.70)	1.07 (0.54 to 2.10)

The "Collective Antidepressants" does not equate to the total of all individual class as some subjects received more than one antidepressant in each class

Exposure time periods:

- 1- Day 1-30: A 30-day risk period starting from the day after the date of prescription.
- 2- Day 31-60: A 30-day risk period starting from day 31 after the date of prescription.
- 3- Day 61-90: A 30-day risk period starting from day 61 after the date of prescription.
- 4- Day 1-90: A 90-day risk period accounts for the entire risk window (day 1 to 90)
- 5- Remainder period: A period starts 90 days after the date of the prescription until the end of the course (from day 91 after date of prescription until the end of the course)
- 6- 90 days washout: A 90-day period starting the day after the end of the course and continuing for 90 days (day 1 after the end of the course until day 90 after the end of the course). Abbreviations: SSRI: Selective Serotonin Reuptake Inhibitor; SNRI: serotonin-norepinephrine reuptake Inhibitor; TCA: Tricyclic antidepressants; MAOI: Monoamine oxidase inhibitors.

Table E5. Age-adjusted incidence rate ratio of COPD exacerbation (excluding cases who died within 6 months following the date of COPD exacerbation) in exposure periods after antidepressant prescription relative to unexposed periods in patients with COPD, calculated by case series analytical technique, UK, 2004-2015

Antidepressant	No. of exposed cases with exacerbation	Day 1-30 IRR (95% CI)	Day 31-60 IRR (95% CI)	Day 61-90 IRR (95% CI)	Day 1-90 IRR (95% CI)	Remainder period IRR (95% CI)	90 days washout IRR (95% CI)
Collective	17,152	1.07 (1.02 to 1.13)	1.12 (1.07 to 1.18)	1.18 (1.11 to 1.26)	1.12 (1.08 to 1.15)	1.30 (1.27 to 1.33)	0.99 (0.93 to 1.07)
Antidepressants							
SSRI or SNRI	10,938	1.07 (1.01 to 1.15)	1.13 (1.06 to 1.20)	1.18 (1.08 to 1.28)	1.12 (1.07 to 1.17)	1.32 (1.28 to 1.36)	1.01 (0.92 to 1.08)
SSRI	10,133	1.05 (0.97 to 1.12)	1.10 (1.03 to 1.18)	1.16 (1.06 to 1.27)	1.09 (1.05 to 1.14)	1.30 (1.25 to 1.34)	1.02 (0.94 to 1.11)
SNRI	1,666	1.11 (0.90 to 1.36)	1.24 (1.05 to 1.47)	1.27 (1.02 to 1.58)	1.19 (1.06 to 1.33)	1.32 (1.23 to 1.43)	1.08 (0.87 to 1.34)
TCA	11,114	1.05 (0.98 to 1.12)	1.12 (1.05 to 1.19)	1.22 (1.12 to 1.32)	1.11 (1.07 to 1.16)	1.21 (1.17 to 1.25)	1.02 (0.95 to 1.11)
MAOI	394	1.10 (0.74 to 1.65)	1.61 (1.16 to 2.23)	1.22 (0.74 to 1.95)	1.37 (1.10 to 1.71)	1.19 (0.93 to 1.52)	0.95 (0.62 to 1.45)

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Exposure time periods:

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- 2- Day 31-60: A 30-day risk period starting from day 31 after the date of prescription.
- 3- Day 61-90: A 30-day risk period starting from day 61 after the date of prescription.
- 4- Day 1-90: A 90-day risk period accounts for the entire risk window (day 1 to 90).
- 5- Remainder period: A period starts 90 days after the date of the prescription until the end of the course (from day 91 after date of prescription until the end of the course)
- 6- 90 days washout: A 90-day period starting the day after the end of the course and continuing for 90 days (day 1 after the end of the course until day 90 after the end of the course). Abbreviations: SSRI: Selective Serotonin Reuptake Inhibitor; SNRI: serotonin-norepinephrine reuptake Inhibitor; TCA: Tricyclic antidepressants; MAOI: Monoamine oxidase inhibitors.

Table E6. Age-adjusted incidence rate ratio of COPD exacerbation (excluding cases who died within 12 months following the date of COPD exacerbation) in exposure periods after antidepressant prescription relative to unexposed periods in patients with COPD, calculated by case series analytical technique, UK, 2004-2015

Antidepressant	No. of exposed cases with exacerbation	Day 1-30 IRR (95% CI)	Day 31-60 IRR (95% CI)	Day 61-90 IRR (95% CI)	Day 1-90 IRR (95% CI)	Remainder period IRR (95% CI)	90 days washout IRR (95% CI)
Collective	16,405	1.07 (1.02 to 1.13)	1.11 (1.05 to 1.16)	1.17 (1.10 to 1.26)	1.12 (1.07 to 1.15)	1.27 (1.24 to 1.30)	0.99 (0.93 to 1.07)
Antidepressants							
SSRI or SNRI	10,472	1.06 (0.99 to 1.14)	1.11 (1.04 to 1.18)	1.19 (1.09 to 1.30)	1.11 (1.06 to 1.16)	1.29 (1.25 to 1.33)	1.01 (0.92 to 1.09)
SSRI	9,696	1.04 (0.96 to 1.11)	1.09 (1.02 to 1.16)	1.17 (1.07 to 1.28)	1.09 (1.04 to 1.14)	1.26 (1.22 to 1.31)	1.06 (0.94 to 1.12)
SNRI	1,609	1.10 (0.89 to 1.36)	1.22 (1.03 to 1.44)	1.24 (0.99 to 1.55)	1.17 (1.04 to 1.31)	1.29 (1.20 to 1.40)	1.08 (0.87 to 1.35)
TCA	10,638	1.05 (0.97 to 1.12)	1.10 (1.03 to 1.17)	1.21 (1.11 to 1.31)	1.10 (1.06 to 1.15)	1.18 (1.13 to 1.22)	1.02 (0.96 to 1.11)
MAOI	381	1.11 (0.75 to 1.63)	1.61 (1.16 to 2.24)	1.27 (0.79 to 1.02)	1.39 (1.11 to 1.74)	1.24 (0.97 to 1.59)	0.96 (0.62 to 1.49)

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Exposure time periods:

- 1- Day 1-30: A 30-day risk period starting from the day after the date of prescription.
- 2- Day 31-60: A 30-day risk period starting from day 31 after the date of prescription.
- 3- Day 61-90: A 30-day risk period starting from day 61 after the date of prescription.
- 4- Day 1-90: A 90-day risk period accounts for the entire risk window (day 1 to 90).
- 5- Remainder period: A period starts 90 days after the date of the prescription until the end of the course (from day 91 after date of prescription until the end of the course)
- 6- 90 days washout: A 90-day period starting the day after the end of the course and continuing for 90 days (day 1 after the end of the course until day 90 after the end of the course). Abbreviations: SSRI: Selective Serotonin Reuptake Inhibitor; SNRI: serotonin-norepinephrine reuptake Inhibitor; TCA: Tricyclic antidepressants; MAOI: Monoamine oxidase inhibitors.

Table E7. The incidence rate ratio of pneumonia (multiple events) after antidepressant prescription relative to unexposed periods in patients with COPD adjusted for age and seasons, calculated by case series analytical technique, UK, 2004-2015

Antidepressants	No. of exposed cases with Pneumonia	Day 1-30 IRR (95% CI)	Day 31-60 IRR (95% CI)	Day 61-90 IRR (95% CI)	Day 1-90 IRR (95% CI)	Remainder period IRR (95% CI)	90 days washout IRR (95% CI)
Collective	1,969	1.79	1.91	2.53	2.10	2.21	1.18
Antidepressants		(1.31 to 2.25)	(1.43 to 2.55)	(1.82 to 2.86)	(1.66 to 2.44)	(1.90 to 2.57)	(0.84 to 1.65)
SSRI or SNRI	1,218	1.87	2.21	3.22	2.43	2.06	1.05
		(1.31 to 2.66)	(1.58 to 3.20)	(2.26 to 3.81)	(1.95 to 2.99)	(1.72 to 2.43)	(0.70 to 1.59)
SSRI	1,143	1.87	2.32	3.44	1.86	1.97	1.30
		(1.30 to 2.69)	(1.63 to 3.31)	(2.43 to 4.86)	(1.54 to 2.4)	(1.64 to 2.36)	(0.89 to 1.88)
SNRI	168	1.30	1.32	1.75	1.20	2.1	1.55
		(0.43 to 3.98)	(0.43 to 4.01)	(0.55 to 5.53)	(0.51 to 2.22)	(1.35 to 3.18)	(0.68 to 3.55)
TCA	1,318	1.53	1.99	1.99	1.75	1.97	1.32
		(1.04 to 2.24)	(1.41 to 2.80)	(1.66 to 2.38)	(1.39 to 2.21)	(1.64 to 2.37)	(0.96 to 1.83)
MAOI	50	0.99	1.10	—	0.79	2.30	2.35
		(0.11 to 9.07)	(0.12 to 10.07)		(0.17 to 3.66)	(0.82 to 6.40)	(0.72 to 7.66)

The “Collective Antidepressants” does not equate to the total of all individual classes as some subjects received more than one antidepressant in each class

Exposure time periods:

- 1- Day 1-30: A 30-day risk period starting from the day after the date of the prescription (segment 1).
- 2- Day 31-60: A 30-day risk period starting from day 31 after the date of the prescription (segment 2).
- 3- Day 61-90: A 30-day risk period starting from day 61 after the date of prescription (segment 3).
- 4- Day 1-90: A 90-day risk period accounts for the entire risk window (day 1 to 90).
- 5- Remainder period: A period starts 90 days after the date of the prescription until the end of the course (from day 91 after date of the prescription until the end of the course).
- 6- 90 days washout: A 90-day period starting the day after the end of the course and continuing for 90 days (day 1 after the end of the course until day 90 after the end of the course). Abbreviations: SSRI: Selective Serotonin Reuptake Inhibitor; SNRI: serotonin-norepinephrine reuptake Inhibitor; TCA: Tricyclic antidepressants; MAOI: Monoamine oxidase inhibitors.

Table E8. The incidence rate ratio of COPD exacerbation (multiple events) in exposure periods after antidepressant prescription relative to unexposed periods in patients with COPD adjusted for age and seasons, calculated by case series analytical technique, UK, 2004-2015

Antidepressants	No. of exposed cases with exacerbation	Day 1-30 IRR (95% CI)	Day 31-60 IRR (95% CI)	Day 61-90 IRR (95% CI)	Day 1-90 IRR (95% CI)	Remainder period IRR (95% CI)	90 days washout IRR (95% CI)
Collective antidepressant	18,483	1.19 (1.06 to 1.32)	1.21 (1.04 to 1.40)	1.29 (1.16 to 1.43)	1.24 (1.17 to 1.34)	1.47 (1.39 to 1.55)	0.99 (0.87 to 1.11)
SSRI or SNRI	11,770	1.03 (0.94 to 1.13)	1.18 (1.10 to 1.28)	1.25 (1.15 to 1.35)	1.15 (1.11 to 1.20)	1.17 (1.09 to 1.22)	1.04 (0.95 to 1.13)
SSRI	10,919	1.01 (0.91 to 1.31)	1.14 (1.01 to 1.27)	1.21 (1.11 to 1.31)	1.13 (1.07 to 1.20)	1.40 (1.35 to 1.46)	1.04 (0.96 to 1.13)
SNRI	1,753	1.13 (0.85 to 1.48)	1.17 (0.95 to 1.49)	1.45 (1.19 to 1.76)	1.28 (1.11 to 1.46)	1.42 (1.30 to 1.56)	1.05 (0.84 to 1.30)
TCA	11,936	1.14 (1.05 to 1.24)	1.18 (1.09 to 1.27)	1.30 (1.24 to 1.36)	1.16 (1.11 to 1.21)	1.19 (1.12 to 1.24)	1.01 (0.93 to 1.10)
MAOI	416	1.17 (0.79 to 1.72)	1.55 (1.10 to 2.20)	1.20 (0.73 to 1.96)	1.32 (1.04 to 1.67)	1.22 (0.94 to 1.58)	0.78 (0.48 to 1.19)

The "Collective Antidepressants" does not equate to the total of all individual classes as some subjects received more than one antidepressant in each class

Exposure time periods:

- 1- Day 1-30: A 30-day risk period starting from the day after the date of the prescription (segment 1).
 - 2- Day 31-60: A 30-day risk period starting from day 31 after the date of the prescription (segment 2).
 - 3- Day 61-90: A 30-day risk period starting from day 61 after the date of prescription (segment 3).
 - 4- Day 1-90: A 90-day risk period accounts for the entire risk window (day 1 to 90).
 - 5- Remainder period: A period starts 90 days after the date of the prescription until the end of the course (from day 91 after date of the prescription until the end of the course 90 days washout).
 - 6- A 90-day period starting the day after the end of the course and continuing for 90 days (day 1 after the end of the course until day 90 after the end of the course).
- Abbreviations: SSRI: Selective Serotonin Reuptake Inhibitor; SNRI: serotonin-norepinephrine reuptake Inhibitor; TCA: Tricyclic antidepressants; MAOI: Monoamine oxidase inhibitors.