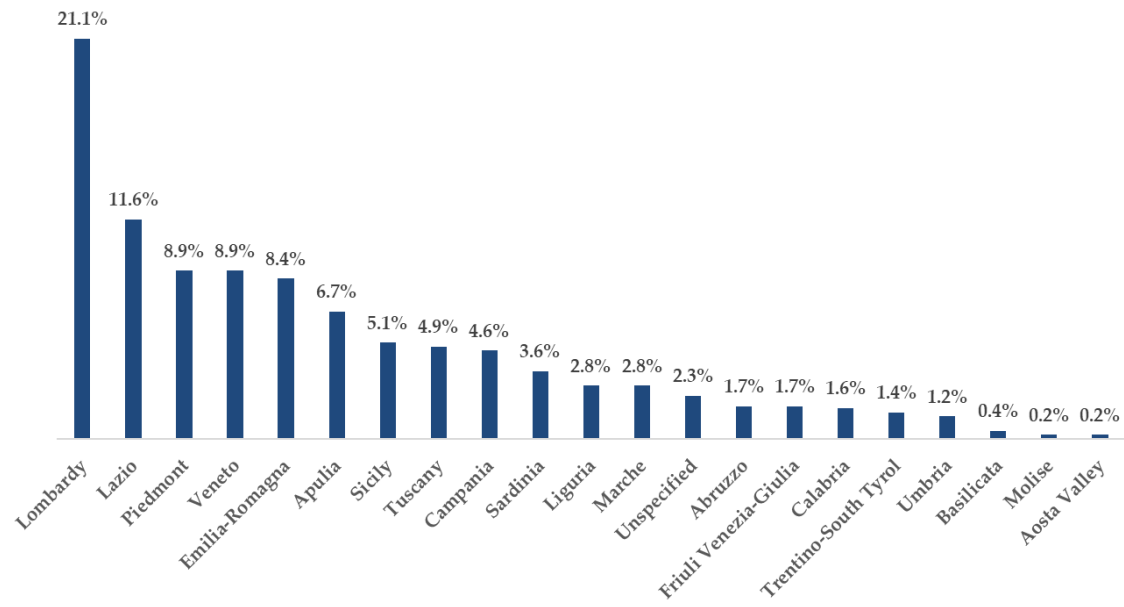
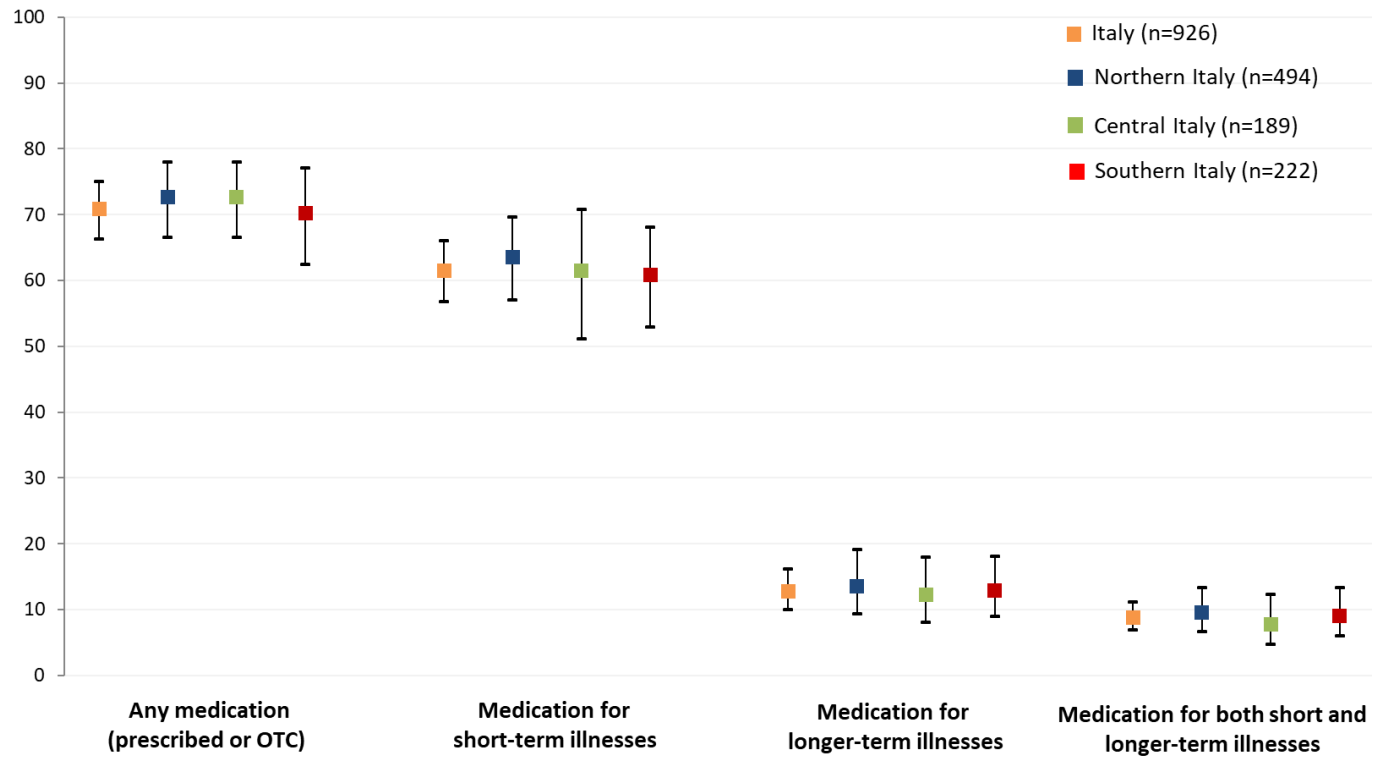


## Supplementary material

Figure S1: Number of responses to the study electronic questionnaires across the regions in Italy



**Figure S2:** Extent of medication used in pregnancy, overall and by treatment of short-term or longer-term illnesses, accordingly to geographical areas (n=926)<sup>1</sup>



<sup>1</sup>Region of residency was missing for 21 women.

Northern Italy includes Lombardy, Piedmont, Trentino-South Tyrol, Aosta Valley, Veneto, Emilia-Romagna, Liguria, Friuli Venezia-Giulia. Central Italy includes Lazio, Marche, Tuscany, Umbria. Southern Italy includes Sicily, Sardinia, Apulia, Molise, Calabria, Basilicata, and Abruzzo.

**Table S1:** Distribution of key indicators of our population versus the birthing population in Italy in 2012 based on CEDAP data[1]

<b>Maternal factors</b>	<b>Study population</b>	<b>Birthing population</b>
	%	%
<b>Age</b>		
< 20	1.2	1.5
20-29	25.5	30.3
30-39	67.0	59.7
40+	6.4	8.5
<b>Educational attainment</b>		
Lower than high school	7.0	30.6
High school	48.7	44.3
More than high school	44.3	25.1
<b>Marital status</b>		
Married or cohabiting	96.8	97.4
Other than above	3.2	2.6
<b>Occupation</b>		
Working	75.3	58.4
Jobless	7.2	9.8
Homemaker	9.0	29.8
Student	2.2	1.6
Other	5.1	0.4
<b>Immigrant status</b>		
No	95.7	80.1
Yes	4.3	19.9

1. Ministry of Health. *Certificate of Delivery Assistance (CEDAP)*. 2012 [cited 2020 1 March]; Available from: [http://www.salute.gov.it/portale/documentazione/p6\\_2\\_2\\_1.jsp?lingua=italiano&id=2768](http://www.salute.gov.it/portale/documentazione/p6_2_2_1.jsp?lingua=italiano&id=2768).

**Table S2:** Overall medication use on 3<sup>rd</sup> with/without 4<sup>th</sup> ATC level, by trimester of use (n=9,459)<sup>1</sup>

Medication by pharmacological subgroup (ATC at 3 <sup>rd</sup> level), with or without 4 <sup>th</sup> level chemical subgroup		Weighted proportions			Unweighted proportions		
		1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester	1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
		n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)
<b>A02A</b>	Antacids	57 6.4 (4.5-9.0)	68 7.5 (5.4-10.2)	75 9.0 (6.6-12.1)	57 6.2 (4.8-7.9)	68 7.3 (5.8-9.2)	75 8.1 (6.5-10.0)
<b>A02AA</b>	Antacids, magnesium compounds	10 1.2 (0.5-2.8)	5 0.8 (0.3-2.6)	<4	10 1.1 (0.6-2.0)	5 0.5 (0.2-1.3)	<4
<b>A02AD</b>	Antacids, aluminium, calcium and magnesium combinations	38 4.5 (1.0-6.9)	52 5.9 (1.1-8.5)	57 7.6 (1.4-10.8)	38 4.1 (3.0-5.6)	52 5.6 (4.3-7.3)	57 6.2 (4.8-7.9)
<b>A02AF</b>	Antacids with antifatulents	<4	5 0.4 (0.2-0.9)	6 0.4 (0.2-1.0)	<4	5 0.5 (0.2-1.3)	6 0.6 (0.3-1.4)
<b>A02AH</b>	Antacids, sodium bicarbonate	12 1.4 (0.6-3.2)	10 1.2 (0.6-3.0)	15 1.6 (0.6-3.4)	12 1.3 (0.7-2.3)	10 1.1 (0.6-2.0)	15 1.6 (1.0-2.7)
<b>A02B</b>	Drugs for peptic ulcer and gastro-esophageal reflux disease	29 4.4 (2.6-7.2)	42 5.9 (3.9-8.8)	38 4.7 (3.0-7.2)	29 3.1 (2.2-4.5)	42 4.5 (3.4-6.1)	38 4.1 (3.0-5.6)
<b>A02BC</b>	Proton pump inhibitors	5 0.4 (0.2-0.9)	4 0.3 (0.1-0.7)	5 0.4 (0.2-0.9)	5 0.5 (0.2-1.3)	4 0.4 (0.2-1.1)	5 0.5 (0.2-1.3)
<b>A02BX</b>	Other drugs for peptic ulcer and gastro-esophageal reflux disease, mainly alginic acid	24 4.0 (2.3-6.9)	38 5.6 (3.6-8.6)	35 4.5 (2.8-7.0)	24 2.6 (1.7-3.8)	38 4.1 (3.0-5.6)	35 3.8 (2.7-5.2)
<b>A03A</b>	Drugs for functional gastrointestinal disorders	10 2.0 (0.8-4.7)	5 0.7 (0.2-2.6)	<4	10 1.1 (0.6-2.0)	5 0.5 (0.2-1.2)	<4
<b>A03AX</b>	Other drugs for functional gastrointestinal disorders, mainly phloroglucinol,	8 1.8 (0.7-4.7)	4 0.6 (0.2-2.6)	<4	8 0.9 (0.4-1.7)	4 0.4 (0.2-1.1)	<4
<b>A03B</b>	Belladonna alkaloids and derivatives	17 2.3 (1.1-4.5)	21 3.0 (1.6-5.5)	11 1.4 (0.6-3.2)	17 1.8 (1.1-2.9)	21 2.3 (1.5-3.5)	11 1.2 (0.7-2.1)
<b>A03BB</b>	Butylscopolamine	17 2.3 (1.1-4.5)	21 3.0 (1.6-5.5)	11 1.4 (0.6-3.2)	17 1.8 (1.1-2.9)	21 2.3 (1.4-3.5)	11 1.2 (0.7-2.1)

Medication by pharmacological subgroup (ATC at 3 <sup>rd</sup> level), with or without 4 <sup>th</sup> level chemical subgroup		Weighted proportions			Unweighted proportions		
		1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester	1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
		n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)
<b>A03F</b>	Propulsives	25 3.0 (1.7-5.2)	10 0.8 (0.4-1.5)	<4	25 2.7 (1.8-4.0)	10 1.1 (0.6-2.0)	<4
<b>A03FA</b>	Metoclopramide or domperidone	25 3.0 (1.7-5.2)	10 0.8 (0.4-1.5)	<4	25 2.7 (1.8-4.0)	10 1.1 (0.6-2.0)	<4
<b>A06A</b>	Drugs for constipation	34 3.7 (2.3-5.7)	52 5.3 (3.8-7.5)	36 3.1 (2.2-4.3)	34 3.7 (2.6-5.1)	52 5.6 (4.3-7.3)	36 3.9 (2.8-5.3)
<b>A06AB</b>	Contact laxatives	4 0.4 (0.1-1.0)	5 0.5 (0.2-1.1)	<4	4 0.4 (0.2-1.1)	5 0.5 (0.2-1.3)	<4
<b>A06AD</b>	Osmotically acting laxatives	16 1.2 (0.7-2.1)	31 3.1 (2.0-4.9)	19 1.7 (1.1-2.6)	16 1.7 (1.1-2.8)	31 3.3 (2.4-4.7)	19 2.1 (1.3-3.2)
<b>A06AG</b>	Enemas	5 0.4 (0.2-0.9)	4 0.3 (0.1-0.9)	4 0.4 (0.1-1.0)	5 0.5 (0.2-1.3)	4 0.4 (0.2-1.1)	4 0.4 (0.2-1.1)
<b>A06AX</b>	Other drugs for constipation (glycerol)	13 1.9 (0.9-4.1)	15 1.6 (0.8-3.1)	9 0.8 (0.4-1.5)	13 1.4 (0.8-2.4)	15 1.6 (1.0-2.7)	9 1.0 (0.5-1.9)
<b>B01A</b>	Antithrombotic agents	13 1.0 (0.6-1.8)	17 1.4 (0.8-2.2)	13 1.0 (0.6-1.7)	13 1.4 (0.8-2.4)	17 1.8 (1.1-2.9)	13 1.4 (0.8-2.4)
<b>B01AB</b>	Heparins	10 0.8 (0.4-1.4)	10 0.8 (0.4-1.5)	7 0.5 (0.2-1.2)	10 1.0 (0.6-2.0)	10 1.1 (0.6-2.0)	7 0.8 (0.4-1.6)
<b>B01AC</b>	Low dose acetylsalicylic acid	7 0.6 (0.3-1.2)	10 0.8 (0.4-1.5)	9 0.7 (0.3-1.3)	7 0.8 (0.4-1.6)	10 1.1 (0.6-2.0)	9 1.0 (0.5-1.9)
<b>G01A</b>	Anti-infective and antiseptic drugs, excluding combinations with corticosteroids	10 0.8 (0.4-1.5)	22 2.5 (1.4-4.4)	17 2.2 (1.1-4.3)	10 1.1 (0.6-2.0)	22 2.4 (1.6-3.6)	17 1.8 (1.1-2.9)
<b>G01AA</b>	Antibiotics	<4	4 0.3 (0.1-0.8)	<4	<4	4 0.4 (0.2-1.1)	<4
<b>G01AF</b>	Imidazole derivatives	9 0.7 (0.4-1.4)	16 2.0 (1.0-4.0)	10 1.2 (0.5-3.1)	9 1.0 (0.5-1.9)	16 1.7 (1.1-2.8)	10 1.1 (0.6-2.0)
<b>H02A</b>	Systemic corticosteroids	4 0.4 (0.1-1.0)	4 0.8 (0.2-3.1)	4 0.8 (0.2-3.1)	4 0.4 (0.2-1.1)	4 0.4 (0.2-1.1)	4 0.4 (0.2-1.1)

Medication by pharmacological subgroup (ATC at 3 <sup>rd</sup> level), with or without 4 <sup>th</sup> level chemical subgroup		Weighted proportions			Unweighted proportions		
		1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester	1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
		n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)
<b>H03A</b>	Thyroid preparations	53 4.6 (3.3-6.4)	43 3.8 (2.6-5.6)	37 3.3 (2.1-5.0)	53 5.7 (4.4-7.4)	43 4.6 (3.5-6.2)	37 4.0 (2.9-5.5)
<b>H03AA</b>	Thyroid hormone, mainly levothyroxine	53 4.6 (3.3-6.4)	43 3.8 (2.6-5.6)	37 3.3 (2.1-5.0)	53 5.7 (4.4-7.4)	43 4.6 (3.5-6.2)	37 4.0 (2.9-5.5)
<b>J01C</b>	Penicillins	16 1.3 (0.8-2.1)	36 4.6 (2.9-7.3)	26 2.9 (1.7-5.0)	16 1.7 (1.1-2.8)	36 3.9 (2.8-5.3)	26 2.9 (1.9-4.1)
<b>J01CA</b>	Penicillins with extended spectrum	11 0.9 (0.5-1.6)	21 2.6 (1.4-4.8)	12 1.8 (0.8-4.0)	11 1.2 (0.7-2.1)	21 2.3 (1.5-3.5)	12 1.3 (0.7-2.3)
<b>J01CR</b>	Penicillins and beta-lactamase inhibitors	5 0.4 (0.2-1.0)	14 2.5 (1.2-5.1)	14 1.5 (0.8-3.1)	5 0.5 (0.2-1.3)	14 1.5 (0.9-2.5)	14 1.5 (0.9-2.5)
<b>J01D</b>	Other beta-lactam antibacterials (mainly third-generation cephalosporins)	-	<4	4 0.4 (0.1-1.0)	-	<4	4 0.4 (0.2-1.1)
<b>J01F</b>	Macrolides	<4	7 1.1 (0.4-3.1)	10 0.8 (0.4-1.5)	<4	7 0.8 (0.4-1.6)	10 1.1 (0.6-2.0)
<b>J01X</b>	Other anti-bacterials	16 1.6 (0.8-3.1)	19 2.3 (1.2-4.2)	14 2.0 (0.9-4.1)	16 1.7 (1.1-2.8)	19 2.1 (1.3-3.2)	14 1.5 (0.9-2.5)
<b>J01XX</b>	Other anti-bacterials, mainly fosfomycin	15 1.5 (0.7-3.0)	19 2.3 (1.2-4.2)	13 1.9 (0.8-4.1)	15 1.6 (1.0-2.7)	19 2.1 (1.3-3.2)	13 1.4 (0.8-2.4)
<b>M01A</b>	NSAID preparations	14 1.0 (0.6-1.7)	7 0.6 (0.3-1.2)	5 0.3 (0.1-0.8)	14 1.5 (0.9-2.5)	7 0.8 (0.4-1.6)	5 0.5 (0.2-1.3)
<b>M01AE</b>	Propionic acid derivates	7 0.5 (0.2-1.1)	<4	<4	7 0.8 (0.4-1.6)	<4	<4
<b>M01AX</b>	Other NSAIDs, mainly nimesulide	4 0.3 (0.1-0.8)	<4	<4	4 0.4 (0.2-1.1)	<4	<4
<b>N02B</b>	Analgesics and antipyretics	206 23.5 (19.7-27.6)	258 30.7 (26.6-35.2)	145 17.5 (14.1-21.5)	206 22.2 (19.7-25.0)	258 27.9 (25.1-30.8)	145 15.7 (13.5-18.1)

Medication by pharmacological subgroup (ATC at 3 <sup>rd</sup> level), with or without 4 <sup>th</sup> level chemical subgroup		Weighted proportions			Unweighted proportions		
		1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester	1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
		n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)
N02BA	Salicylic acid and derivatives, mainly high dose acetylsalicylic acid	5 0.3 (0.1-0.8)	<4	<4	5 0.5 (0.2-1.3)	<4	<4
N02BE	Anilides, mainly paracetamol	202 23.2 (19.5-27.4)	191 24.1 (21.2-28.5)	144 17.4 (14.1-21.3)	202 21.8 (19.3-24.6)	191 20.6 (18.1-23.4)	144 15.6 (13.4-18.0)
N02C	Antimigraine drugs	5 1.3 (0.4-4.1)	5 1.3 (0.4-4.1)	<4	5 0.5 (0.2-1.3)	5 0.5 (0.2-1.3)	<4
N05B	Anxiolytics	11 1.3 (0.6-2.9)	9 0.8 (0.4-1.5)	4 0.4 (0.1-1.0)	11 1.2 (0.7-2.1)	9 1.0 (0.5-1.9)	4 0.4 (0.2-1.1)
N05BA	Benzodiazepine derivatives	10 1.3 (0.6-2.9)	9 0.8 (0.4-1.5)	4 0.4 (0.1-1.0)	10 1.1 (0.6-2.0)	9 1.0 (0.5-1.9)	4 0.4 (0.2-1.1)
N06A	Antidepressants	11 1.3 (0.6-2.9)	10 0.8 (0.4-1.5)	9 0.7 (0.3-1.3)	11 1.2 (0.7-2.1)	10 1.1 (0.6-2.0)	9 1.0 (0.5-1.9)
N06AB	SSRI antidepressants	8 1.0 (0.4-2.7)	6 0.4 (0.2-1.0)	5 0.3 (0.1-0.8)	8 0.9 (0.4-1.7)	6 0.6 (0.3-1.4)	5 0.5 (0.2-1.3)
R01A	Sympathomimetic nasal decongestants	12 1.0 (0.5-1.7)	17 1.3 (0.8-2.1)	11 1.5 (0.6-3.6)	12 1.3 (0.7-2.3)	17 1.8 (1.1-2.9)	11 1.2 (0.7-2.1)
R01AA	Plain sympathomimetic nasal decongestants	8 0.6 (0.3-1.3)	11 0.8 (0.4-1.5)	6 1.2 (0.4-3.5)	8 0.9 (0.4-1.7)	11 1.2 (0.7-2.1)	6 0.6 (0.3-1.4)
R01AB	Combination of sympathomimetic nasal decongestants, excluding corticosteroids	<4	6 0.5 (0.2-1.2)	<4	<4	6 0.6 (0.3-1.4)	<4
R01AD	Corticosteroids	<4	4 0.3 (0.1-0.8)	<4	<4	4 0.4 (0.2-1.1)	<4
R03A	Inhalant adrenergics	9 0.9 (0.4-1.7)	8 1.2 (0.5-3.1)	7 1.0 (0.3-3.0)	9 1.0 (0.5-1.9)	8 0.9 (0.4-1.7)	7 0.8 (0.4-1.6)
R03AC	Inhalant selective beta-2 agonists	6 0.6 (0.3-1.3)	7 1.1 (0.4-3.1)	5 0.8 (0.2-3.0)	6 0.6 (0.3-1.4)	7 0.8 (0.4-1.6)	5 0.5 (0.2-1.3)

Medication by pharmacological subgroup (ATC at 3 <sup>rd</sup> level), with or without 4 <sup>th</sup> level chemical subgroup		Weighted proportions			Unweighted proportions		
		1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester	1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester	3 <sup>rd</sup> trimester
		n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)	n % (95% CI)
<b>R03B</b>	Other inhalant drugs for COPD	4 0.3 (0.1-0.9)	6 0.6 (0.2-1.2)	4 0.3 (0.1-0.9)	4 0.4 (0.2-1.1)	6 0.6 (0.3-1.4)	4 0.4 (0.2-1.1)
<b>R03BA</b>	Glucocorticoids	4 0.3 (0.1-0.9)	6 0.6 (0.2-1.2)	4 0.3 (0.1-0.9)	4 0.4 (0.2-1.1)	6 0.6 (0.3-1.4)	4 0.4 (0.2-1.1)
<b>R05C</b>	Expectorants	<4	10 0.7 (0.4-1.3)	5 0.4 (0.2-1.0)	<4	10 1.1 (0.6-2.0)	5 0.4 (0.2-1.3)
<b>R05CB</b>	Mucolytics, mainly acetylcysteine	<4	10 0.7 (0.4-1.3)	5 0.4 (0.2-1.0)	<4	10 1.1 (0.6-2.0)	5 0.5 (0.2-1.3)
<b>R06A</b>	Systemic antihistamines	<4	4 0.3 (0.1-0.9)	<4	<4	4 0.4 (0.2-1.1)	<4
<b>Total medication use (any ATC)</b>		<b>394</b> <b>43.9 (39.5-48.4)</b>	<b>411</b> <b>47.1 (42.7-51.6)</b>	<b>289</b> <b>31.1 (27.1-35.4)</b>	<b>394</b> <b>42.5 (39.4-45.8)</b>	<b>411</b> <b>44.4 (41.2-47.7)</b>	<b>289</b> <b>31.2 (28.3-34.3)</b>

Abbreviations: NSAID=Non-steroidal anti-inflammatory drugs; SSRI=Selective serotonin re-uptake inhibitors; COPD=Chronic obstructive pulmonary disease.

<sup>1</sup>Only medication groups with at least 4 exposed pregnancies in one of the trimester are presented. Numbers less than 4 are presented as "<4". Point estimate by 4<sup>th</sup> ATC level are presented only when there are at least 6 exposed to the 3<sup>rd</sup> level ATC medication group. Timing of medication exposure is defined as follows: 1st trimester (gestational weeks 0-12), 2nd trimester (gestational week 13-24), 3rd trimester (gestational week 25 and up to childbirth).