

**Table S1. Geographical distributions of general physicians' (GPs) characteristics from 2000 to 2019**

	2000							
LHU	Milano City	Insubria	Montagna	Brianza	Bergamo	Brescia	Val Padana	Pavia
Age, years, mean (SD)	47.3 (8.2)	47.1 (7.6)	47.3 (6.6)	47.1 (7.3)	47.1 (7.3)	47.1 (7.3)	48.0 (6.9)	47.1 (7.2)
Sex, Male, n (%)	1805 (68.6)	740 (71.0)	207 (79.6)	613 (72.5)	559 (75.0)	544 (73.8)	423 (75.0)	317 (76.8)
Patients in charge, median (IQR range)	702 (433-857)	693 (457-824)	657.5 (457-776.5)	719 (437-841)	705 (460-803)	740 (524-837)	739 (518.5-869)	711 (451-874)
Proportion of older patients in charge ( $\geq 65$ years), median (IQR range)	33.5 (27.4-39.2)	33.5 (28.9-37.6)	34.1 (30.0-38.0)	31.4 (26.9)	30.7 (26.3-35.6)	32.2 (27.5-36.6)	37.3 (32.4-41.8)	38.6 (33.9-42.6)
Proportion of patients with polypharmacy therapy in charge, median (IQR range)	17.5 (13.8-21.5)	15.5 (12.2-19.5)	15.2 (10.6-20.6)	16.0 (12.9-19.2)	18.3 (15.0-22.1)	19.6 (15.9-23.6)	19.2 (15.4-22.6)	19.7 (16.0-23.9)
Mean number of different antibiotics prescribed per patient in the year, median (IQR range)	1.9 (1.8-2.0)	1.9 (1.7-2.0)	1.8 (1.7-2.1)	1.9 (1.8-2.0)	2.0 (1.8-2.1)	2.0 (1.9-2.2)	1.8 (1.7-1.9)	2.0 (1.8-2.1)
Mean number of DDD of antibiotics prescribed per patient in the years, median (IQR range)	41.0 (35.2-47.5)	38.9 (33.7-45.9)	39.5 (33.9-47.6)	40.4 (34.8-46.9)	40.1 (34.1-47.5)	41.6 (35.1-47.7)	36.8 (32.2-43.1)	41.3 (35.7-49.0)
Mean number of antibiotic refill for month per patient, median (IQR range)	1.3 (1.2-1.5)	1.3 (1.2-1.5)	1.3 (1.1-1.5)	1.4 (1.2-1.6)	1.4 (1.2-1.6)	1.4 (1.2-1.5)	1.3 (1.1-1.5)	1.4 (1.3-1.6)
Mean number of antibiotic switches for month per patient, median (IQR range)	1.2 (1.1-1.3)	1.2 (1.1-1.3)	1.2 (1.1-1.3)	1.2 (1.1-1.3)	1.2 (1.1-1.3)	1.2 (1.1-1.3)	1.2 (1.1-1.3)	1.3 (1.2-1.4)
	2010							
Age, years, mean (SD)	54.6 (5.7)	54.5 (5.9)	55.0 (6.2)	54.9 (5.7)	54.4 (5.7)	54.4 (5.7)	55.1 (5.6)	54.3 (5.8)
Sex, Male, n (%)	1512 (64.6)	670 (67.4)	188 (76.7)	539 (69.2)	515 (70.6)	507 (69.4)	378 (70.5)	310 (73.1)
Patients in charge, median (IQR range)	913 (675-1029)	885.5 (654-990)	819 (642-951)	930 (737-1016)	899 (260.5-899)	924 (750-1003)	897.5 (692-1006.5)	838 (546.5-1004.5)
Proportion of older patients in charge ( $\geq 65$ years), median (IQR range)	35.7 (30.4-40.6)	35.0 (31.0-38.9)	35.2 (31.3-37.8)	34.3 (30.2-38.1)	31.8 (27.6-36.0)	33.5 (28.3-38.0)	36.4 (32.7-40.1)	37.5 (33.1-41.9)
Proportion of patients with polypharmacy therapy in charge, median (IQR range)	23.7 (19.3-28.3)	22.8 (18.9-26.6)	23.0 (19.5-26.5)	23.1 (19.9-27.1)	22.8 (19.3-26.7)	25.3 (20.8-29.0)	26.6 (23.2-30.8)	25.9 (22.5-30.3)
Mean number of different antibiotics prescribed per patient in the year, median (IQR range)	1.9 (1.8-2.1)	1.9 (1.8-2.0)	1.9 (1.8-2.1)	1.9 (1.8-2.1)	1.9 (1.8-2.1)	2.1 (1.9-2.2)	1.9 (1.8-2.0)	2.0 (1.9-2.1)
Mean number of DDD of antibiotics prescribed per patient in the years, median (IQR range)	21.4 (14.1-25.9)	22.1 (15.9-27.1)	19.0 (0-25.5)	21.6 (12.7-26.5)	21.2 (10.5-25.8)	21.1 (14.9-25.8)	20.2 (13.1-23.8)	21.3 (11.9-26.0)
Mean number of antibiotic refill for month per patient, median (IQR range)	1.2 (0-1.4)	1.2 (1-1.4)	1.2 (0-1.4)	1.2 (1.0-1.4)	1.2 (0-1.4)	1.2 (1.0-1.4)	1.2 (0.0-1.4)	1.3 (0.0-1.4)
Mean number of antibiotic switches for month per patient, median (IQR range)	1.1 (0.0-1.2)	1.1 (1.0-1.2)	1.0 (0.0-1.2)	1.1 (0.0-1.2)	1.1 (0.0-1.2)	1.1 (1.0-1.2)	1.1 (0.0-1.2)	1.2 (0.0-1.3)
	2018							
Age, years, mean (SD)	59.6 (7.5)	59.4 (7.5)	58.4 (8.9)	59.3 (8.1)	58.9 (7.8)	57.6 (9.3)	60.4 (7.6)	59.6 (7.6)
Sex, Male, n (%)	1427 (60.1)	611 (61.8)	154 (71.3)	501 (63.8)	476 (66.4)	488 (63.9)	364 (68.2)	284 (67.6)
Patients in charge, median (IQR range)	1011 (756-1095)	991 (758-1072)	992 (846.5-1071)	1027 (865-1091)	984 (815-1056)	985.5 (827-1059)	961.5 (756-1063)	919.5 (561.5-1073)
Proportion of older patients in charge ( $\geq 65$ years), median (IQR range)	37.1 (31.6-41.2)	37.7 (33.1-41.2)	38.1 (35.3-41.6)	37.2 (32.2-40.8)	35.4 (30.4-39.2)	35.8 (30.6-40.0)	38.5 (34.0-42.1)	38.7 (33.0-42.7)
Proportion of patients with polypharmacy therapy in charge, median (IQR range)	25.8 (20.1-30.5)	24.7 (20.3-28.7)	25.3 (21.9-29.4)	25.9 (21.1-30.0)	25.6 (21.4-29.8)	25.5 (21.2-29.4)	29.7 (25.2-34.3)	29.8 (25.7-34.4)
Mean number of different antibiotics prescribed per patient in the year, median (IQR range)	1.3 (1.2-1.3)	1.3 (1.2-1.3)	1.3 (1.2-1.3)	1.3 (1.2-1.3)	1.3 (1.2-1.3)	1.3 (1.2-1.3)	1.3 (1.2-1.3)	1.3 (1.2-1.3)
Mean number of DDD of antibiotics prescribed per patient in the years, median (IQR range)	24.1 (20.4-28.4)	25.3 (21.4-29.3)	23.8 (19.9-27.6)	24.9 (21.0-29.2)	24.4 (21.0-28.7)	24.0 (20.9-28.2)	22.8 (19.9-26.4)	23.9 (20.4-28.3)

Mean number of antibiotic refill for month per patient, median (IQR range)	1.3 (1.2-1.4)	1.3 (1.2-1.5)	1.2 (1.2-1.6)	1.3 (1.2-1.5)	1.3 (1.2-1.5)	1.4 (1.2-1.5)	1.3 (1.2-1.5)	1.4 (1.2-1.5)
Mean number of antibiotic switches for month per patient, median (IQR range)	1.2 (1.1-1.2)	1.2 (1.1-1.3)	1.2 (1.1-1.3)	1.1 (1.1-1.29)	1.2 (1.1-1.2)	1.2 (1.1-1.3)	1.2 (1.1-1.2)	1.2 (1.1-1.3)
	<b>2019</b>							
Age, years, mean (SD)	60.2 (7.7)	59.9 (8.0)	58.5 (9.3)	59.6 (8.6)	59.5 (8.0)	58.1 (9.4)	60.5 (8.3)	60.2 (7.8)
Sex, Male, n (%)	1386 (59.4)	600 (61.1)	126 (67.7)	483 (62.9)	463 (65.3)	473 (64.1)	354 (66.5)	271 (66.4)
Patients in charge, median (IQR range)	1075.5 (819-1154)	1037 (773-1112)	1024 (885-1096)	1067 (901-1128)	1014 (851-1083)	1022 (881-1089)	1000 (771.5-1104)	984.5 (579-1121)
Proportion of older patients in charge ( $\geq 65$ years), median (IQR range)	36.7 (31.0-40.9)	37.5 (32.5-40.8)	38.4 (35.3-41.8)	37.2 (32.0-40.8)	35.5 (30.3-39.5)	35.9 (30.1-39.7)	38.0 (33.0-42.0)	37.7 (31.0-42.4)
Proportion of patients with polypharmacy therapy in charge, median (IQR range)	24.4 (18.8-29.3)	23.9 (19.5-28.0)	25.4 (22.2-29.3)	25.1 (20.9-29.5)	25.2 (20.6-29.2)	24.3 (20.1-28.8)	28.9 (23.7-33.6)	29.4 (25.0-33.5)
Mean number of different antibiotics prescribed per patient in the year, median (IQR range)	1.8 (1.6-1.9)	1.8 (1.7-1.9)	1.8 (1.7-2.0)	1.8 (1.7-1.9)	1.8 (1.7-1.9)	1.9 (1.8-2.0)	1.8 (1.7-1.9)	1.9 (1.7-2.0)
Mean number of DDD of antibiotics prescribed per patient in the years, median (IQR range)	32.2 (26.1-37.6)	33.4 (27.3-38.7)	30.0 (21.2-36.8)	32.2 (25.4-38.1)	33.0 (25.0-38.7)	32.4 (10.5-38.4)	29.8 (22.3-35.1)	31.9 (26.0-38.5)
Mean number of antibiotic refill for month per patient, median (IQR range)	1.3 (1.1-1.5)	1.3 (1.1-1.5)	1.3 (1.1-1.5)	1.3 (1.1-1.5)	1.3 (1.0-1.5)	1.3 (0.0-1.5)	1.3 (1.0-1.5)	1.4 (1.2-1.6)
Mean number of antibiotic switches for month per patient, median (IQR range)	1.1 (1.0-1.2)	1.1 (1.0-1.3)	1.1 (1.0-1.3)	1.1 (1.0-1.2)	1.1 (1.0-1.2)	1.2 (1.1-1.3)	1.1 (1.0-1.2)	1.2 (1.1-1.3)

LHU: Local Health Unit; IQR: Inter Quartile Range; DDD: Defined Daily Dose