Opinion about seasonal influenza vaccination among the general population 3 years after the A(H1N1)pdm2009 influenza pandemic

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Keywords

Influenza, Vaccination, Epidemiological factors, Population surveillance

Highlights

- In France, 39% reported a positive opinion regarding seasonal flu vaccination

- 39% and 22%reported a neutral and a negative opinion

- Healthy young adults were more inclined to have neutral or negative opinions

-As well as those preferring homeopathic treatments

- And those who did not work in contact with elderly or sick individuals

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Abstract

*Objective:*Toassess theopinions of the French general population aboutseasonal influenza vaccinationthree years after the A(H1N1)pdm 09 pandemic and identify factors associated with a neutral or negative opinion aboutthis vaccination.

*Study design:*The study was conducted using data collected from 5374 participants during the 2012/2013 season of the GrippeNet.fr study. The opinion about seasonal influenza vaccination was studied on three levels ("positive", "negative" or "neutral"). The link between the participant's characteristics and their opinion regarding the seasonal influenza vaccination were studied using a multinomial logistic regression with categorical variables. The "positive" opinion was used as the reference for identifying individuals being at risk of having a "neutral" or a "negative" opinion.

*Results:*Among the participants, 39% reported having a positive opinion about seasonal influenza vaccine, 39% a neutral opinion, and 22% a negative opinion. Factors associated with a neutral or negative opinion were young age, low educational level, lack of contact with sick or elderly individuals, lack of treatment for a chronic disease and taking a homeopathic preventive treatment.

*Conclusions:*These results show that an important part of the French population does not have a positive opinion about influenza vaccination in France.Furthermore, it allows outlining the profiles of particularly reluctant individuals who could be targeted by informative campaigns.

Introduction

According to the World Health Organization(WHO), seasonal influenza is a major cause of morbidity and mortality worldwide, and is responsible for 3 to 5 million serious illnesses and for 250,000 to 500,000 deaths each year, depending on virulence and epidemic duration (1). In France, influenza is the reason for 700,000 to 4.8 million influenza-like-illnesses (ILI) consultations each year, which represents 1to 8 % of the general population (2, 3), and 0.3 (± 0.6) to 4 (± 2.8) work days lost per person and per influenza episode (4). Mortality is difficult to estimate because it includes influenza related deaths, but also deaths recorded for other reasons such as "pneumonia" or "cardiovascular diseases"(5). Thus, it is estimated from 0 to 24 deaths per 100,000 inhabitants and per flu epidemic from 1972 to 2010 (6), whereindividualsaged over 65 accounted for 90% of deaths (7, 8).

Vaccination isthe main preventive measure advocated by the WHOagainst influenza. In France vaccination is recommended for individuals at risk of developing complicated forms of diseases likeindividuals over age 65, pregnant women, obese individuals, healthcare workers, and individuals living with a chronic disease for 6 months or more (9). Vaccination of these groups remains a major public health concern withthe objective to reachan immunization coverage of 75% in 2015 (10).

The vaccination campaign management during the 2009 influenza pandemic A(H1N1) appears to have strongly affected the acceptability of vaccination among the French population, particularly vaccination against seasonal influenza. During the pandemic, several studies wereconductedin France to assessperceptions of the A(H1N1)pdm09 vaccine in the general population(11), as well as among health professionals (12-15). The main results revealedexistingdoubts aboutthe severity of the pandemic, the safety and efficacy of thevaccine adjuvant, and the role of the physician in

patients' adherence to the vaccination. Similar results were also obtained in other countries(16-22).

The campaign of 2009 resulted in France with only 7.9% of the general population being vaccinated, contrary to expectations for a larger coverage (23). A study published in 2012 showeda decrease in influenza vaccination coverage among "at risk" populations between 2009 and the two subsequent seasons 2010 and 2011 (59.8%, 50.4% and 51.0% of vaccination coverage rates respectively)(24). This decrease was validated by the National Security Agency of Medicines and Health Products (ANSM), which indicated a decrease of 19.7% in the seasonal flu vaccines distribution between 2009 and 2010 (24).

In view of the aforementioned data,the objectivesof this study were to assess theseasonal influenza vaccine acceptability among the general population and factors associated with this acceptability, three years after the 2009 pandemic.

Materials and methods

The study was conducted using data collected inthe cohort *GrippeNet.fr*, a web-based participative study conducted in France(25).Developed by the French National Institute of Health and Medical Research (Inserm), Pierre and Marie Curie University (UPMC) and the French Institute for Public Health Surveillance (InVS), this project is part of a broader European study,Influenzanet (http://www.influenzanet.eu)(26), whichallows monitoring ILI evolution directly in the general population.The inclusion criteria to participate in the GrippeNet.fr study include: 1) residency in France 2) comprehension of the French language 3) access to the Internet. Upon registration, participants were asked to complete a baseline questionnaire covering demographic factors (age, gender), geographicalfactors (location of home and work/school expressed at themunicipality level), socio-economic factors (household size and composition, occupation, educational level, number of daily contacts with groups of patients, children or elderly, daily transportation means),

and health-related factors (height and weight, diet, vaccination status, pregnancy status, smoking habits,major risk conditions, and opinion about seasonal influenza vaccination evaluated over three levels ("positive", "negative" or "neutral").Subsequently, they were invited to describe weekly clinical symptoms during the flu season. From November 2012 to April 2013, 6059 individualsin France voluntarily contributed to the data collection for GrippeNet.frThe representativeness of the participants was recently published elsewhere (25).The GrippeNet.fr population was not representative of the general population in terms of age and gender, however all ageclasses were represented, including the older classes (65+ years old), generally less familiar with the digital world, butconsidered at higher risk for influenza complications. Once adjusted on demographic indicators, the GrippeNet.fr populationwas found to be more frequently employed, with a higher education level and vaccination rate with respect to the generalpopulation. A similar propensity to commute for work to different regions was observed, and no significant difference wasfound for asthma and diabetes.

Study population

From the GrippeNet.fr participant pool, those above 18 years who completed the baseline questionnaire for the 2012/2013 season (November 2012-April 2013) were included in the study. This amounts to 5374 of the 6059 GrippeNet.fr participants; 659 children, 19 persons who didn’t specify their ages,and 7 persons living outside Francewere excluded from the study.

Data analysis

A description of the population included in the study was conducted and outlierswereverified, corrected or excluded as needed.The opinion about seasonal influenza vaccinationwas studied usingthe three levels proposed in the baseline questionnaire ("positive", "negative" or "neutral").The link between the participant’scharacteristics and their opinion regarding the seasonal influenza vaccination was studied using a multinomial logistic regressionwith categorical

variables. The "positive"opinionserved asthe reference foridentifyingindividualsbeing at risk of having a "neutral" or a "negative" opinion. Explanatory variables included socio-demographic characteristics (age, sex, educational level, main activity, presence of children in the household), contacts during a typical day (children, old individuals, sick individuals); geographical characteristics (place of residence)and clinical characteristics. According to the national French recommendations (9), anew variable named "At risk group for influenza" was created, defined by individuals with at least one of the following characteristics: age ≥ 65 years, body mass index (BMI) ≥ 40, pregnancy or having received aninfluenza vaccination voucher from the French government, which include patients with a chronic underlying disease. The effect of each explanatory variable was studied using univariateanalysesfirst, then multivariate analyses. Allvariables that had a p-value less than 0.2 in univariate analyses were included in the multivariate analyses. In multivariate analysis, two variables were deliberately excluded: the vaccination status variableand the variable dealing with individuals being at risk of having complicated influenza,as they were too correlatedwith the other variables of interest. Each odds ratiowas obtained from a step down multinomial logistic regression with categorical variables, using a 95% confidence interval. All statistical analyses were performed using the R software.

Results

Population's characteristics

The study population consisted of 2018 men (38%) and 3356 women (62%), with amean age of50 years (Table 1). For the educational level,1569 participants (37%) had at least a Masters degree and664 participants (16%) had an educational level below theBachelorsdegree. Regarding employment, 2300 participants (43%) were employedfull-timeand 1417 (26%) were retired. All regions were represented.Most participants were living in medium size urban cities: 1373 persons (25.5%) lived in cities with 2,000 to 10,000 habitants and 1833 (34%) in cities with10,000 to

100,000 inhabitants. Vaccination coverage against seasonal influenza was estimated to be28% (n=1515) in the study population. Among the participants, 1636 (31%) had at least one risk factor for complicated influenza and among them, 897 (55%) were vaccinated against influenza.

Opinion regarding influenza seasonal vaccinationand associated factors

In our study, 2037 participants (39%) had a positive opinion regardinginfluenza seasonalvaccination, 2052 participants (39%) had a neutral one and 1167 participants (22%) a negative one. Among individuals≥ 65 years old, 554 (55%) had a positive opinion regarding influenza seasonal vaccination, 273 (27%) had a neutral one and 179 (18%) a negative one.

In multivariate analysis (Tables 2a-2b), factors significantly associated with neutral opinion comparedto a positive opinion about influenza seasonal vaccinationwere: having 35-50 yearsold comparedto 18-35 years old(OR, 0.72; 95% CI,0.57-0.91), having at least 65 years old comparedto 18-35 years old(OR, 0.28; 0.18-0.43), taking a treatment for chronic diseases (OR, 0.48; 0.37-0.62), taking preventive homeopathic treatment during the winter season (OR, 3.29; 2.70-4.00), the frequency of colds orILI, contact with elderly (OR, 0.70; 0.52-0.94) or contact with patients (OR, 0.57; 0.45-0.72), at least one child from 5 to18 years in the household(OR, 0.76; 0.62-0.95), being a student rather than an employee (OR, 1.54; 1.04-2.28), having a low study level, living in medium-size cities (OR, 0.68; 0.54-0.86) and living in some regions.

Factors significantly associated with a negative opinion rather than a positive one about seasonal flu vaccines(Tables 2a-2b) were:having 50-65 yearsold compared to 18-35 years old(OR, 0.56; 0.41-0.77), having at least 65 years old compared to 18-35 years old(OR, 0.38; 0.23-0.61), obesity (BMI ≥ 40) (OR, 2.23; 1.02-4.87), taking treatment for a chronic disease (OR, 0.54; 0.40-0.72), taking preventive homeopathic treatment during the winter season (OR, 4.85; 3.84-6.14), the frequency of ILI or colds, daily contact with patients (OR, 0.54; 0.40-0.73) , at least one 5-18

years old child in the household"(OR, 1.26; 1.03-1.53), having a low study level and living in certain regions.

Discussion

This work provides an overview of the opinions about influenza seasonal vaccination in the general population using data from GrippeNet.fr study, as well as factors related to a negative or neutral opinion of thisvaccination.

In the study, almost a quarter of participants reported a negative opinion of influenza seasonal vaccination and 39% a neutral one. To our knowledge, few studies haveaddressed the question of opinions onvaccination against the seasonal flu. Most studies addressvaccination acceptability based onimmunization coverage rates of: healthcare workers (12, 27, 28), individualstargeted by the recommendations (29-31) or the general population (28, 32, 33). In France the Health Barometer has studied the acceptability of influenza vaccinations from a similar perspective. A recent study(34)focused on changes in attitude of 18 to 75 years old Frenchindividualsregarding vaccination by comparing Health Barometer studiescarried outin 2000, 2005 and 2010 (data collected between October 2009 to June 2010 for the last one). This study showed a strong increase in adverse opinions against vaccination in general: 8.5% in 2000, 9.6% in 2005 and 38.2% in 2010. In 2010, 47% reported a negative opinion for at least one type of influenzavaccination (based on 3 possible and non-exclusive answers: 42.1% for the vaccination against the A(H1N1)pdm09pandemic influenza, 7.7% for the influenza seasonal vaccination, and 5.7% for influenzavaccination in general) (unpublished Inpes data). Although there has been no Health Barometer since 2010,the gradual decrease of the vaccination coverage rate against influenza among individualsat risk of complications(24) suggests that vaccine reluctancehas increased in recent years. Vaccination coverage rateagainst seasonal flu among at risk individuals was 50.1% in 2012-2013 (respectively 51.8 % and 51.7% in 2010/2011 and 2011/2012) which

reveals a gradual decrease since 2009/2010 (60.2%) (35). This decrease in the flu vaccination coverage rates is also observed in Spain (27), Switzerland (36), Germany (37), whereasthe situation is more nuanced in the UK (38). In the United States an isolated decrease of the vaccination coverage rate was observed among adults in 2011/2012 (39).

In this study, we highlighted factors associated with opinion on flu vaccination for the general population and not only on at risk individuals currently targeted by recommendations. It allowsoutlining theprofiles linked with neutral or negative opinion regardingflu vaccination. Individualsmore inclined to have neutral or negative opinions were healthy young adults, those preferring homeopathy and those who did not work in contact with elderly or sickindividuals. This profile appeared similar to those of parents of children from 6 to 59 months of age targeted by the most recent WHO flu vaccine recommendations (40), independently of the fact that children may be at risk of complication. This suggeststhat it may be difficult to implement such a measure in France. In Europe, only Finland has implemented a vaccination program for young children, the UK planned to do the samefor children ages2-17 years old (41). Other countries, like the United States, recommend the vaccination of the entire population from 6 months of age (42). Even if the immunization schedule was simplified in 2013 in France(9),it stillprovides a large number of vaccinations in young children. The addition of a new yearly vaccine against influenza in this age groupseems to be particularly difficult.

Individuals with a severe obesityhad a more frequently negative opinion of the influenza vaccine, even though they have been targeted by the vaccine recommendations since 2010 (Notice HCSP 29/12/2010). This resistance towards theinfluenza vaccination is confirmed by a lowvaccination coverage ratein this group (around 25%)(43). It is difficult for the NationalHealth Insurance to obtain theBMI of patients in orderto send them a vaccination voucher and appropriate information. Health professionals and the media are, as a result, responsible for vaccinationpromotion.

However, when looking at the posters and leaflets of the last immunization campaigns(44-46), we observed that the focus was primarily on the elderly and patients with chronic diseases. Obese individuals are mentioned in several documents, but are not directly targeted by these campaigns. The results of the study also suggestthat information on the influenza vaccine should be targeted more widelynot restricting it only to individuals at risk, but also considering social characteristics for example,students, as already successfully tested in the USA(47), or individuals with a low education level, who are more likely tohavea negative opinion of theflu vaccine.

Even if our assumptions are consistent with the literature, this study has some limitations.First of all, our population is not fully representative of the French population (25). A web-based participative study may have inhibited the participation of certain individuals(such asthe elderly orindividuals of low social status); there is also a risk of over-representation of individualssensitive to health issues or adverse to vaccination. The Internet is however becoming more important and pervasive in our daily lives, regardless of age; hence itoffers the opportunity to reach an increasinglylarger number of individuals. Taking into account opinions on vaccinationas the main criterion for the decision and not theact of vaccinationitself allowed us to study the general population and not only targeted individuals. Renewal of studies using this same criterion would allow a better assessment of how the opinion evolvesamong different groups of thegeneral population in France, and provide the information needed for a more efficient and prompt reaction before such evolutionhas an impact on thevaccination coverage rate.

Finally,opinions regarding vaccinationagainstseasonal influenzahave changedin the general populationsince theA(H1N1)pdm2009pandemicinfluenza witha significant increase inthe number of individuals with a negative opinion andagradual decline invaccination coverage rateamong at riskindividuals. Further studies areneeded to better understandthepsychosocialmechanisms underlyingthis change ofopinionwith the aim of conductingtargeted and adaptivecommunication

campaigns. Apart fromthe decline inprotectionof individualsat riskofcomplicatedinfluenza duringseasonal epidemics, the major risk is a rejection of vaccination by the general population inthe event of another influenza pandemic, with importanthealth and social consequences.

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Conflict of interest statement

Authors have nothing to disclose.

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Table 1: Participants characteristics (N=5374)

Characteristics	Results
Age, mean [quartile]	50.5 [38 ; 62.5]
Male, n (%)	2018 (38)
Level of education, n (%)	
Lower than High School certificate	664 (16)
High School certificate or equivalent	764 (18)
Bachelor degree	1239 (29)
Master degree or higher	1569 (37)
Main activity, n (%)	
Full-time employment	2300 (43)
Part-time employment	525 (10)
Self-employed	298 (5.5)
Student	297 (5.5)
Home-maker (e.g. housewife)	207 (4)
Unemployed	184 (3)
Long-term sick-leave or Parental leave	93 (2)
Retired	1417 (26)
Place of residence, n (%)	
Rural	1032 (19)
Urban – Isolated Town	401 (7.5)
Urban - Suburbs	2036 (38)
Urban - City	1905 (35.5)
Population of the municipality, n (%)	
< 200	93 (1.5)
[200 - 2,000)	1009 (19)
[2000 - 10,000)	1373 (25.5)
[10,000 - 100,000)	1833 (34)
[100,000 - 1.000,000)	745 (14)
≥ 1.000,000	321 (6)
At- risk group for influenza, n (%) *	1636 (31)
Asthma, n (%) **	330 (6)
Other Chronic diseases, n (%) ***	736 (14)
Receiving seasonal flu vaccine (season 2012/2013), n (%)	1515 (28)
Influenza preventive homeopathic treatment, n (%)	1133 (21)

* At least one criteria between Age ≥ 65 years, BMI ≥ 40, pregnancy, voucher reception for influenza vaccination

** Regular medication for asthma

*** Regular medication for chronic diseases like diabetes, chronic lung disorder (besides asthma), heart disorder, kidney disorder, acquired immune deficiency

Table 2a:Factors associated with the influenza vaccination opinion (multivaried analysis)

Variables	N	Positive Opinion n (%)	Neutral Opinion n (%)	Neutral OpinionvsPositive Opinion OR (IC 95%)	p value	Negative Opinion n (%)	Negative Opinion vs Positive Opinion OR (IC 95%)	p value
Age								
18 to 35 years	995	269 (27)	498 (50)	1 (reference)		228 (23)	1 (reference)	
35 to 49 years	1582	540 (34)	662 (42)	**0.72 (0.57 ; 0.91)**	**0.007**	380 (24)	0.85 (0.65 ; 1.12)	0.28
50 to 64 years	1673	674 (40)	619 (37)	**0.48 (0.36 ; 0.63)**	**<0.001**	380 (23)	**0.56 (0.41 ; 0.77)**	**<0.001**
≥ 65 years	1006	554 (55)	273 (27)	**0.28 (0.18 ; 0.43)**	**<0.001**	179 (18)	**0.38 (0.23 ; 0.61)**	**<0.001**
BMI categories								
[18 to 25)	3127	1160 (37)	1264 (40.5)	1 (reference)		703 (22.5)	1 (reference)	
< 18	122	39 (32)	55 (45)	1.08 (0.65 ; 1.80)	0.76	28 (23)	0.87 (0.47 ; 1.60)	0.65
[25 to 30)	1381	601 (43.5)	506 (36.5)	0.96 (0.81 ; 1.15)	0.64	274 (20)	0.88 (0.71 ; 1.09)	0.24
[30 to 40)	492	197 (40)	179 (36.5)	1.13 (0.86 ; 1.48)	0.39	116 (23.5)	1.15 (0.84 ; 1.57)	0.39
≥ 40	53	18 (34)	15 (28)	1.16 (0.51 ; 2.65)	0.72	20 (38)	**2.23 (1.02 ; 4.87)**	**0.05**
Regular medication for asthma								
No	4933	1882 (38)	1942 (39.5)	1 (reference)		1109 (22.5)	1 (reference)	
Yes	323	155 (48)	110 (34)	**0.68 (0.50 ; 0.94)**	**0.01**	58 (18)	**0.62 (0.43 ; 0.90)**	**0.01**
Regular medication for other chronic diseases								
No	4540	1619 (36)	1870 (41)	1 (reference)		1051 (23)	1 (reference)	
Yes	716	418 (58.5)	182 (25.5)	**0.48 (0.37 ; 0.62)**	**<0.001**	116 (16)	**0.54 (0.40 ; 0.72)**	**<0.001**
Colds or Flu-like diseases frequency								
Never	1057	386 (36.5)	406 (38.5)	1 (reference)		265 (25)	1 (reference)	
Occasionally, not every year	1319	531 (40)	520 (39.5)	0.91 (0.72 ; 1.16)	0.5	268 (20.5)	**0.73 (0.55 ; 0.96)**	**0.02**
Once or twice a year	1963	773 (39.5)	757 (38.5)	**0.75 (0.60 ; 0.93)**	**0.01**	433 (22)	**0.68 (0.54 ; 0.86)**	**0.001**
More than 3 times a year	845	319 (37.5)	345 (41)	**0.71 (0.55 ; 0.92)**	**0.01**	181 (21.5)	**0.61 (0.46 ; 0.82)**	**0.001**
Influenza preventive homeopathic treatment								
No	3414	1570 (46)	1235 (36)	1 (reference)		609 (18)	1 (reference)	
Yes	1105	223 (20)	486 (44)	**3.29 (2.70 ; 4.00)**	**<0.001**	396 (36)	**4.85 (3.84 ; 6.14)**	**<0.001**
Don't know	732	243 (33)	328 (45)	**1.68 (1.36 ; 2.09)**	**<0.001**	161 (22)	**1.73 (1.34 ; 2.24)**	**<0.001**

Table 2b:Factors associated with the influenza vaccination opinion (multivaried analysis)

Variables	N	Positive Opinion n (%)	Neutral Opinion n (%)	Neutral Opinion vs Positive Opinion OR (IC 95%)	p value	Negative Opinion n (%)	Negative Opinion vs Positive Opinion OR (IC 95%)	p value
≤ 1 child between 5-18 years old in the household								
No	3696	1495 (40.5)	1384 (37.5)	1 (reference)		817 (22)	1 (reference)	
Yes	1560	542 (34.5)	668 (43)	**0.76 (0.62 ; 0.95)**	**0.02**	350 (22.5)	**1.26 (1.03 ; 1.53)**	**0.03**
Daily contacts with > 10 individuals aged ≥ 65								
No	4760	1800 (38)	1900 (40)	1 (reference)		1060 (22)	1 (reference)	
Yes	496	237 (48)	152 (30.5)	**0.70 (0.52 ; 0.94)**	**0.01**	107 (21.5)	0.89 (0.64 ; 1.24)	0.49
Daily contacts with patients								
No	4591	1718 (37.5)	1842 (40)	1 (reference)		1031 (22.5)	1 (reference)	
Yes	665	319 (48)	210 (31.5)	**0.57 (0.45 ; 0.72)**	**<0.001**	136 (20.5)	**0.54 (0.40 ; 0.73)**	**<0.001**
Level of Education								
Master Degree or higher	1536	659 (43)	602 (39)	1 (reference)		275 (18)	1 (reference)	
Bachelor degree	1206	418 (35)	495 (41)	**1.46 (1.23 ; 1.74)**	**<0.001**	293 (24)	**1.79 (1.44 ; 2.22)**	**<0.001**
High School Certificate or equivalent	744	264 (35.5)	281 (38)	**1.43 (1.13 ; 1.81)**	**0.002**	199 (26.5)	**2.08 (1.58 ; 2.73)**	**<0.001**
Lower than High School Certificate	643	197 (30.5)	269 (42)	**1.92 (1.48 ; 2.47)**	**<0.001**	177 (27.5)	**2.64 (1.97 ; 3.54)**	**<0.001**
Main Activity								
Full-time employment	2247	810 (36)	956 (42.5)	1 (reference)		481 (21.5)	1 (reference)	
Part-time employment	509	167 (33)	202 (39.5)	1.03 (0.80 ; 1.33)	0.81	140 (27.5)	1.27 (0.95 ; 1.71)	0.10
Self-employed	296	126 (42.5)	94 (32)	0.83 (0.58 ; 1.18)	0.28	76 (25.5)	1.36 (0.94 ; 1.98)	0.11
Student	290	67 (23)	162 (56)	**1.54 (1.04 ; 2.28)**	**0.04**	61 (21)	1.21 (0.74 ; 1.97)	0.42
Home-maker (e.g. housewife)	204	63 (31)	89 (43.5)	0.99 (0.67 ; 1.47)	0.95	52 (25.5)	0.89 (0.55 ; 1.42)	0.62
Unemployed	182	50 (27.5)	77 (42.5)	1.19 (0.74 ; 1.90)	0.97	55 (30)	1.54 (0.92 ; 2.56)	0.10
Long-term sick-leave or Parental leave	90	26 (29)	31 (34.5)	1.01 (0. 51 ; 2.01)	0.97	33 (36.5)	**2.10 (1.06 ; 4.16)**	**0.04**
Retired	1386	714 (51.5)	420 (30.5)	0.88 (0.63 ; 1.23)	0.43	252 (18)	0.68 (0.46 ; 1.00)	0.053
Population (number of inhabitants)								
[10 000. 100 000)	1796	667 (37)	744 (41.5)	1 (reference)		385 (21.5)	1 (reference)	
< 200	92	39 (42.5)	35 (38)	0.85 (0.41 ; 1.76)	0.07	18 (19.5)	0.68 (0.32 ; 1.45)	0.31
[200 – 2,000)	989	374 (38)	367 (37)	0.80 (0.63 ; 1.02)	0.06	248 (25)	1.00 (0.76 ; 1.32)	0.97
[2,000 – 10,000)	1338	524 (39)	514 (38.5)	0.87 (0.71 ; 1.06)	0.18	300 (22.5)	0.90 (0.71 ; 1.13)	0.36
[100,000 – 1. 000,000)	728	304 (42)	270 (37)	**0.68 (0.54 ; 0.86)**	**0.002**	154 (21)	0.76 (0.57 ; 1.02)	0.07
≥ 1.000,000	313	129 (41)	122 (39)	0.95 (0.67 ; 1.35)	0.78	62 (20)	1.09 (0.71 ; 1.68)	0.68