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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: To assess the opinions of the French general population about seasonal influenza vaccination three years after the A(H1N1)pdm 09 pandemic and identify factors associated with a neutral or negative opinion about this 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 1 to 8 % of the general population (2, 3), and 0.3 (\pm 0.6) to 4 (\pm 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), where individuals aged over 65 accounted for 90% of deaths (7, 8).

Vaccination is the main preventive measure advocated by the WHO against influenza. In France vaccination is recommended for individuals at risk of developing complicated forms of diseases like individuals 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 with the objective to reach an 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 were conducted in France to assess perceptions of the A(H1N1)pdm09 vaccine in the general population(11), as well as among health professionals (12-15). The main results revealed existing doubts about the severity of the pandemic, the safety and efficacy of the vaccine 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 showed a 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 objectives of this study were to assess the seasonal 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 in the 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.influenza.net.eu>)(26), which allows 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), geographical factors (location of home and work/school expressed at the municipality 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 individuals in France voluntarily contributed to the data collection for GrippeNet.fr. The 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 age classes were represented, including the older classes (65+ years old), generally less familiar with the digital world, but considered at higher risk for influenza complications. Once adjusted on demographic indicators, the GrippeNet.fr population was found to be more frequently employed, with a higher education level and vaccination rate with respect to the general population. A similar propensity to commute for work to different regions was observed, and no significant difference was found 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 France were excluded from the study.

Data analysis

A description of the population included in the study was conducted and outliers were verified, corrected or excluded as needed. The opinion about seasonal influenza vaccination was studied using the three levels proposed in the baseline questionnaire ("positive", "negative" or "neutral"). The link between the participant's characteristics and their opinion regarding the seasonal influenza vaccination was studied using a multinomial logistic regression with categorical

variables. The "positive" opinion served as the reference for identifying individuals being 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), a new 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 an influenza vaccination voucher from the French government, which include patients with a chronic underlying disease. The effect of each explanatory variable was studied using univariate analyses first, then multivariate analyses. All variables 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 variable and the variable dealing with individuals being at risk of having complicated influenza, as they were too correlated with the other variables of interest. Each odds ratio was 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 a mean age of 50 years (Table 1). For the educational level, 1569 participants (37%) had at least a Masters degree and 664 participants (16%) had an educational level below the Bachelors degree. Regarding employment, 2300 participants (43%) were employed full-time and 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 with 10,000 to

100,000 inhabitants. Vaccination coverage against seasonal influenza was estimated to be 28% (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 vaccination and associated factors

In our study, 2037 participants (39%) had a positive opinion regarding influenza seasonal vaccination, 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 compared to a positive opinion about influenza seasonal vaccination were: having 35-50 years old compared to 18-35 years old (OR, 0.72; 95% CI, 0.57-0.91), having at least 65 years old compared to 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 or ILI, 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 to 18 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 years old 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 this vaccination.

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 have addressed the question of opinions on vaccination against the seasonal flu. Most studies address vaccination acceptability based on immunization coverage rates of: healthcare workers (12, 27, 28), individuals targeted 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 French individuals regarding vaccination by comparing Health Barometer studies carried out in 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 influenza vaccination (based on 3 possible and non-exclusive answers: 42.1% for the vaccination against the A(H1N1)pdm09 pandemic influenza, 7.7% for the influenza seasonal vaccination, and 5.7% for influenza vaccination 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 individuals at risk of complications(24) suggests that vaccine reluctance has increased in recent years. Vaccination coverage rate against 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), whereas the 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 allows outlining the profiles linked with neutral or negative opinion regarding flu vaccination. Individuals more 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 sick individuals. 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 suggests that 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 same for children ages 2-17 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 still provides a large number of vaccinations in young children. The addition of a new yearly vaccine against influenza in this age group seems to be particularly difficult.

Individuals with a severe obesity had 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 the influenza vaccination is confirmed by a low vaccination coverage rate in this group (around 25%) (43). It is difficult for the National Health Insurance to obtain the BMI of patients in order to send them a vaccination voucher and appropriate information. Health professionals and the media are, as a result, responsible for vaccination promotion.

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 suggest that information on the influenza vaccine should be targeted more widely not 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 to have a negative opinion of the flu 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 as the elderly or individuals of low social status); there is also a risk of over-representation of individuals sensitive to health issues or adverse to vaccination. The Internet is however becoming more important and pervasive in our daily lives, regardless of age; hence it offers the opportunity to reach an increasingly larger number of individuals. Taking into account opinions on vaccination as the main criterion for the decision and not the act of vaccination itself 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 evolves among different groups of the general population in France, and provide the information needed for a more efficient and prompt reaction before such evolution has an impact on the vaccination coverage rate.

Finally, opinions regarding vaccination against seasonal influenza have changed in the general population since the A(H1N1)pdm2009 pandemic influenza with a significant increase in the number of individuals with a negative opinion and a gradual decline in vaccination coverage rate among at risk individuals. Further studies are needed to better understand the psychosocial mechanisms underlying this change of opinion with the aim of conducting targeted and adaptive communication

campaigns. Apart from the decline in protection of individuals at risk of complicated influenza during seasonal epidemics, the major risk is a rejection of vaccination by the general population in the event of another influenza pandemic, with important health 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 Opinion vs Positive 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

