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Flu vaccination coverage in Italy in the COVID-19 era: A fuzzy functional k-means (FFKM) approach

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ABSTRACT

Background: In Europe, flu vaccination coverage has decreased, and there are complex barriers to overcome to vaccinate against flu. Many studies have been conducted to estimate vaccination coverage. The COVID-19 pandemic threatens to disrupt immunization programs in many countries, including Italy, where vaccination against the flu is recommended but not mandatory. This paper aims to understand changes in flu vaccine uptake in Italian regions.
Methods: Using functional data analysis and fuzzy functional k-means clustering, we investigated changes in flu vaccine coverage in Italian regions before (2010–2019) and after (2020–2022) the COVID-19 vaccination period.
Results: The period of COVID-19 pandemic brought an increase in vaccine coverage globally. Elbow's method determined that the optimal number of clusters in vaccination uptake is 2. Apulia, Basilicata, Emilia Romagna, Liguria, Molise, Tuscany, and Umbria in 2019 belong less to the group with low flu vaccination uptake (G1) but increase their tendency to belong to this group over time: they decrease their propensity to be vaccinated for flu. For others, it seems that COVID-19 served as a push to increase flu vaccination coverage rates. Sicily appears to be the region that has responded best to the pandemic, changing its membership value from 2019 to 2022.
Conclusion: The present study highlights that the COVID-19 era has resulted in a higher flu vaccination coverage rate. Moreover, the regional level's improvement or worsening in flu vaccination coverage rate is not affected by the historical gap and socio-cultural and economic differences prevailing among Italian regions.

Introduction

Flu is a common, highly contagious respiratory virus infecting all ages. Every year about 5.0–15.0 % of the worldwide population experience seasonal flu, with 3.5 million severe cases and more than 500,000 deaths [1,2]. In Europe, flu vaccination coverage recently decreased to below 50 % in 2014 [3]. In Europe, the latest available vaccination coverage data refer to the 2014–2015 season and reveal an average of 45.5 % (range of 1.0–76.3 %) among the elderly; 24.0 % (5.0–54.9 %) in healthcare workers; 49.8 % (21.0–71.8 %) for chronically ill populations, and 23.6 % (0.3–56.1 %) in pregnant women [2,4]. There are complex barriers to overcome to vaccinate against the flu, as knowledge of the vaccine is not always enough to guarantee its acceptance [5]. It may be beneficial to provide additional information to people studying healthcare; this information would be intended to mitigate safety concerns and increase the pressure of social assistance to promote the uptake of healthcare and vaccination in this population. Many studies have been conducted to estimate vaccination coverage [6–8]. In recent years, given the COVID-19 and the related vaccination campaigns, it could be interesting to understand whether those who vaccinate for COVID-19 tend to no longer vaccinate for flu or, on the contrary, are more likely to do so than in the years before the pandemic. Flu vaccination protects people from flu-related illness, reducing the burden on national health systems as COVID-19 spreads and public health measures to control respiratory viral infections ease. However, maintaining flu vaccination services is challenging because the COVID-19 pandemic threatens to disrupt immunization programs in many countries [9]. In Italy, vaccination against the flu is recommended but not

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mandatory [10,11]. The COVID-19 pandemic, with the temporary forced block of many health activities, including vaccinations and the fear of contagion in attending healthcare environments (especially during the first pandemic wave), has undoubtedly significantly impacted vaccination coverage rates [12]. In Italy, the COVID-19 pandemic has caused a sharp slowdown in immunization activities, particularly for vaccinations not included among the mandatory ones [12]. In the ten years before COVID-19, in Italy, flu vaccination coverage rate fluctuated in the interval 13.8 %–19.9 %. Hence, in all the Italian regions, since 2010, flu vaccination coverage has been very low compared to the expectations of vaccination campaigns (75–80 %) [13–15]. Infection with one pathogen does not preclude coinfection with second or more pathogens. Thus, flu strains will circulate in conjunction with COVID-19. Therefore, with the current strains of these two viruses, the clinical outcome is not significantly worse than infection with COVID-19 alone. However, several strains of flu circulate, including strains still to come. Similarly, COVID-19 has several strains, with probably more to come[16]. Immunization programs can reduce the burden due to preventable infectious diseases and decrease related morbidity, mortality, and healthcare costs; however, in Italy, the loss of confidence towards vaccination resulted in low vaccine coverage[17,18]. In all countries, there is interest in the effect of the COVID-19 pandemic on flu vaccination. The geographical distribution of the studies is as follows: Asia (China [19,20], Hong Kong[21], Kuwait [3], Japan [22]), Europe (France [23], Greece [22,24–26], Cyprus [25], Ireland [27], Italy [28–31], Malta [32], Poland [33], Spain [34]), Turkey [35], United Kingdom [36], and United States [37–43].

This paper investigated the changes in flu vaccine coverage rate at the state-population level (males and females older than five months) before and after COVID-19 (from January 2010 to January 2022) in Italian regions. Due to the functional nature of the data, functional data analysis (FDA) is used to reconstruct the flu vaccination coverage rate trends for each region. Then, the fuzzy functional k-means (FFKM) clustering was performed before, during and after the COVID-19 vaccination period to understand the behaviour of Italian regions regarding flu vaccination coverage considering the effect of the COVID-19 vaccination.

Materials and methods

Data sources and participants

The data are collected using the Health for All (HFA) software [44]. HFA is provided by the World Health Organization and has been adapted for national needs by the Italian National Institute of Statistics (ISTAT). We collect Italian regions' flu vaccine coverage time series from 2010 to 2022. The data are calculated considering the number of flu vaccinations on the resident population on the 1st of January of each year. In particular, the value for Trentino-South Tyrol was obtained as a weighted average of the values for the provinces of Bolzano and Trento (Trentino-South Tyrol is an autonomous region in the northern part of Italy, and it is composed of two provinces).

Statistical analysis

In the past few decades, numerous researchers worldwide have taken a keen interest in both functional data analysis (FDA) [45–52] and fuzzy set theory [42], delving into both their methodologies and practical applications. Notably, FDA has prompted renowned mathematicians and statisticians, particularly recently, to reframe a substantial portion of conventional statistical approaches using functional concepts. Essentially, FDA constitutes a facet of statistics relating to scenarios where the presented data exhibit functions rather than conventional numerical values or vectors. Frequently, FDA has been employed to examine dynamic phenomena over time, accomplished through techniques like data smoothing. Our framework uses the FDA approach to reconstruct the Italian regions' vaccination coverage functions. Thus, the first step of this approach is to convert the original time observations into functional objects through a suitable smoothing technique. A basis function system achieves the transition from individual time observations for each regional function. In this context, we have focused on using b-splines (using six interior knots [45]). The procedure aims to synthesise data using a function expressed as a linear combination of basis functions (e.g. fixed basis as the b-splines or data-driven basis like functional principal components):

$$y(t) = \sum_{j=1}^{K} c_j \varphi_j(t) \tag{1}$$

where c_j is the vector of coefficients defining the linear combination and $\varphi_j(t)$ is the vector of K basis functions (j = 1,., K). Thus, $y(t)$ represents a function, i.e. a curve that simultaneously considers all the values observed in a region during the observed period; this function can be treated as a single entity.

In the literature, numerous basis functions have been proposed to handle diverse types of data, such as B-splines, Fourier basis, wavelets, and polynomials. Nonetheless, in the subsequent sections of this study, our focus centers on the functional principal component decomposition (FPCA) that is used to reduce dimensionality while retaining the utmost information content from the original dataset. FPCA enables the representation of functions through a linear combination of a limited number of functional principal components (FPCs) (see e.g. [47,51,53]). Several metrics and semi-metric can be used in the functional context to calculate the distance between curves. One possible semi-metric is precisely the one that considers the proximity between functions based on FPCs [52].

On the other hand, fuzzy clustering, is an approach in data analysis that focuses on dividing a set of data into groups or clusters so that each data point can belong to more than one cluster with some degree of membership instead of belonging exclusively to a single cluster as is the case in traditional clustering. In the context of fuzzy clustering, each data point is associated with a membership vector that contains fuzzy values that indicate the degree of membership of that point in each cluster [54]. These membership values can range from 0 to 1 and reflect how representative a point is of a given group. Fuzzy clustering is especially useful when the boundaries between clusters aren't sharp and clearly defined, or when a data point may have characteristics that make it partially similar to multiple clusters. This approach is often used in applications where data can be interpreted nuanced or uncertainly, such as consumer preference analysis, image segmentation, and the analysis of relationships in biological data. A typical algorithm for implementing fuzzy clustering is the Fuzzy K-Means (FKM), which extends the traditional K-Means to incorporate the concept of fuzzy membership [54]. The FKM is an unsupervised classification algorithm proposed by Bezdek [54] in the non-functional context and extended to the functional framework by Maturo et al. [42].

In the classical FKM initial phase, the researcher selects the number of groups c to cluster the n units using p features to compute dissimilarities among statistical units. The algorithm proceeds iteratively through the minimization of an objective function: J_m. The objective function has to be minimised by calculating the optimal values of the degrees of membership. This depends on both the distance d_{ik}, between the i-th unit and the centroid of the k-th group, and the parameter m that adjusts the level of fuzziness:

$$\mathrm{Jm}(\mathrm{U}, \mathrm{v}) = \sum_{k=1}^{c} \sum_{i=1}^{n} (u_{ik})^{m} (d_{ik})^{2} \tag{2}$$

$d_{ik} = ||x_i - v_k||$ is a suitable norm on R^p, $v \in R^p$ is the component k-th of the centroid vector, $x_i \in R^p$ is the component i-th of units

Table 1
Raw data, mean and standard deviation (SD) of the Flu Vaccination percentage coverage of the Italian regions and absolute difference between 2019 and 2020. Δ= difference.

Regions	Geoghraphical area	2019	2020	2021	2022	Δ (2022 vs 2019)
Abruzzo	South	15.2	16.4	17.9	21.2	6.0
Aosta Valley	North	13.3	13.8	18.8	16.5	3.2
Apulia	South	17.0	17.8	25.6	24.9	7.9
Basilicata	South	18.8	17.3	19.0	22.4	3.6
Calabria	South	15.1	16.3	23.5	21.5	6.4
Campania	South	15.9	16.7	21.9	19.4	3.5
Emilia-Romagna	North	17.5	18.9	26.1	22.9	5.4
Friuli-Venezia Giulia	North	18.9	20.3	25.8	20.4	1.5
Latium	Centre	15.5	16.2	27.5	22.0	6.5
Liguria	North	18.5	19.9	31.3	24.8	6.3
Lombardy	North	12.9	13.7	19.4	18.5	5.6
Marche	Centre	16.5	18.1	26.1	21.6	5.1
Molise	South	18.9	20.0	22.4	19.2	0.3
Piedmont	North	15.3	16.4	21.9	18.8	3.5
Sardinia	South	14.2	15.2	23.7	15.4	1.2
Sicily	South	16.0	18.1	26.5	22.4	6.4
Trentino - South Tyrol	North	12.3	12.1	19.4	12.8	0.5
Tuscany	Centre	19.1	20.1	28.2	21.8	2.7
Umbria	Centre	19.4	19.8	26.9	23.6	4.2
Veneto	North	16.0	16.3	21.6	17.7	1.7
Overall Mean ± SD		**16.3 ± 2.1**	**17.2 ± 2.3**	**23.7 ± 3.6**	**20.4 ± 3.1**	**4.1 ± 2.2**

vector, U[u_{ik}] is the matrix of the degree of membership of size $n \times c$ and $m \in [1,\infty)$. The degree of membership u_{ik} of the i units to the k group satisfies the following constraints:

$$0 \le u_{ik} \le 1 \quad (3)$$

$$\sum_{k=1}^{c} u_{ik} = 1 \quad (4)$$

where i = 1,…n, and k = 1,…c. The array U, of size n x c, contains the degrees of membership u_{ik}.

In the FDA context, using the semi-metric of the FPCs of the smoothed functions, we use an extension of the FKM, i.e. the Fuzzy Functional *K*-Means (FFKM) clustering [42], on the scores of the FPCs [42] before (from 2010 to 2019), during and after the start of the COVID-19 vaccinations begin in Italy (from 2020 to 2022) [53,55]. As a result, we obtain a clustering of the curves so that each function belongs to each group with a different "*degree of truth*", without requiring them to belong to a group uniquely. The advantage of the FFKM is to provide additional information for the study of the dynamics of phenomena in the long term. The previous algorithm is extended to the field of FDA using functions derived using proper smoothing techniques, e.g., b-splines or FPCs, as in Eq. 1.

The FFKM identifies similar behaviours at the regional level but embraces the uncertainty that the fuzzy functional classification preserves in results. Compared to the classical functional k-means approach, the FFKM has the advantage of not forcing units to belong to a single cluster and thus leaving unexplored areas of time where functions are more similar than others. The Elbow method was used to choose the number of groups. All the analyses are performed by using the R statistical environment (version 4.3). The R packages used for the study are "*fda*" [52] and "*fda.usc*" [48] with suitable adaptations of the code to implement fuzzy clustering.

Results

Table 1 shows the raw flu vaccine coverage rate data in the Italian regions from 2019 to 2022 and their differences. In 2019, there was a flu vaccination coverage rate in Italy of 16.3 % ± 2.1 % in SD (Table 1). Thus, in Italy, the average vaccination coverage rate in 2020 was approximately 17 %, and in 2021 it was about 24 % (Table 1). Fig. 1 Panel A shows the trend of vaccination coverage rates from 2010 until 2019 (before the pandemic of COVID-19). Fig. 1 (Panel B) adds one year to Fig. 1 (Panel A) and thus includes the years until 2020; Fig. 1 (Panel C) shows the coverage rate until 2021, where it can already be seen that the rates have a surge except for some regions: Apulia, Basilicata, Calabria, Campania, Emilia-Romagna, Liguria, Molise, Tuscany, Umbria, and Veneto. Globally, for all the Italian regions, the COVID-19 pandemic increased vaccine coverage. However, considering the attitude of these regions since 2010, it is interesting to understand how they improved their performance in terms of flu vaccination coverage rates over time and how, despite socio-cultural, economic, etc., disparities, they behave in the same way.

Fig. 1 (Panel D) provides the graphical representation using FDA and then with the b-spline basis encompassing the time up to 2022. From 2021–2022, after a general peak, the vaccination coverage rate began to decline in almost all regions, moving across Italy from an average flu vaccination coverage rate of 24 % to a rate of approximately 20 % (Table 1).

Fig. 2 (Panel A, B, C, D) reports the FFKM results and shows how Italian regions are affected by the COVID-19 pandemic. The optimal number of clusters is set to two using Elbow's method. In FFKM, all the statistical units belong to all the groups with some degree of membership; however, a pattern of two distinct groups (red and green) is evident. The red curves represent the group with the regions with the highest vaccination rate (G2). In contrast, the regions whose flu vaccination rate functions are green (G1) have a lower vaccination rate. Few regions belong to G1 and G2 with a degree of membership of approximately 0.5, and thus they assume a very "fuzzy behaviour". This justifies using the FFKM because otherwise, with a crisp method, we would have forced them to belong to a group that doesn't fully characterize them.

Table 1 shows the degrees of membership in Group 1 (G1) before (2019) and after the advent of COVID-19 (2020, 2021 and 2022). Apulia, Basilicata, Emilia Romagna, Liguria, Molise, Tuscany, and Umbria in 2019 belong less to G1 instead of G2 but increase their tendency to belong to G1 over time: they decrease their propensity to be vaccinated for flu. For others, it seems that COVID-19 served as a push to increase flu vaccination coverage rates. Sicily, in particular, appears to be the region that has responded best to the pandemic period changing its membership value from 2019 to 2022 by 4.0 %. Indeed, the latter goes from a vaccination coverage rate of 16.0 % in 2019, 18.1 % in 2020, 26.5 % in 2021, and 22.4 % in 2022 (Table 1).

Table 2 shows the change in belonging to G1 and highlights that Apuglia, Basilicata, Calabria, Campania, Emilia-Romagna, Tuscany, Umbria, Veneto, Liguria, and Molise worsened in terms of flu vaccine

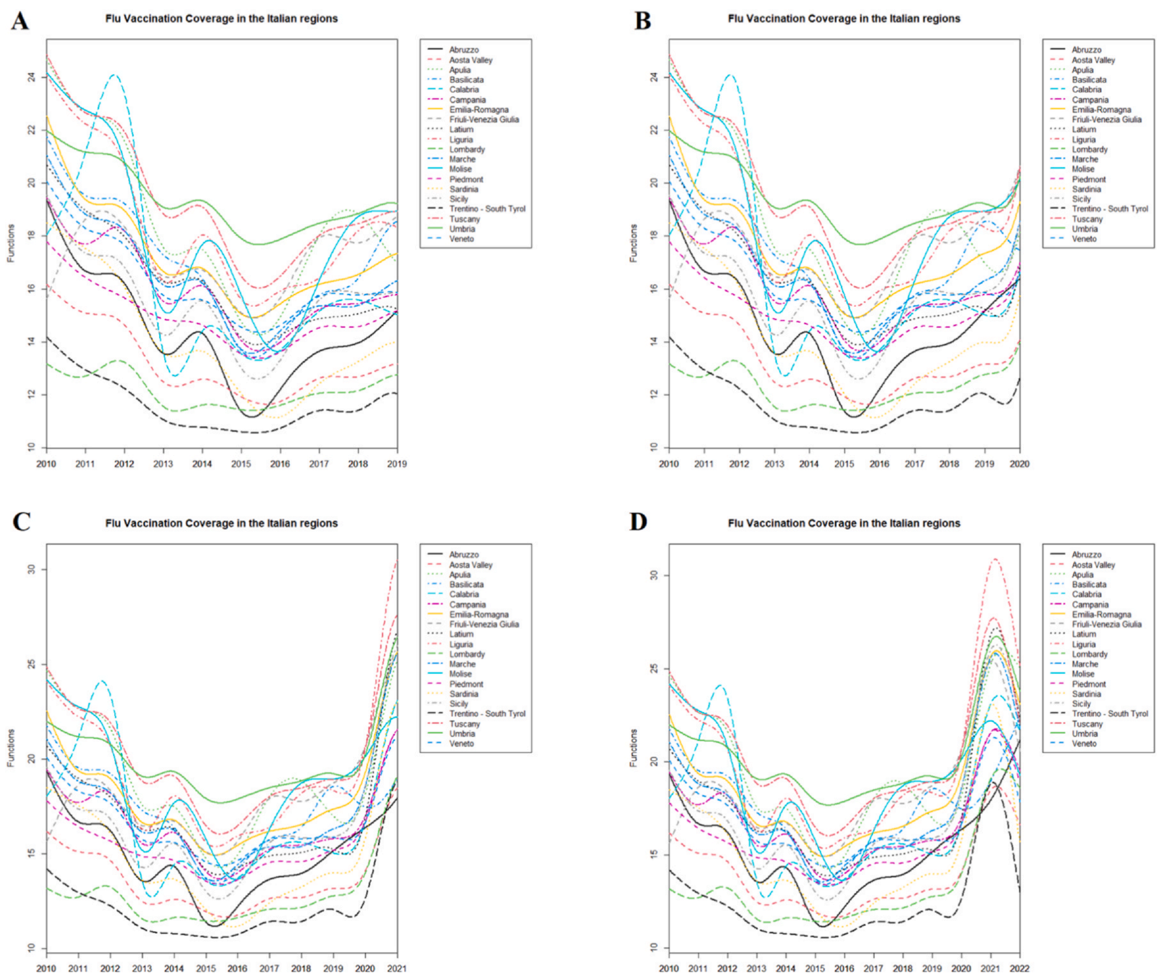

Fig. 1. The smoothed functional Flu Vaccination coverage of the Italian regions using b-splines and six interior knots (setting up a basis system with a knot at every data point).

coverage. In contrast, the remaining ten regions undergo an improvement by decreasing their degree of G1 membership.

Fig. 3 depicts the change over time (2019 vs 2022) of the membership value for each Italian region to G1, showing how, in the COVID-19 era, regions changed, in summary, their attitude to be inclined to vaccinate. We can state that ten regions (red ones) change their behaviour regarding flu vaccination coverage decreasing their membership value to G1 (the group with lower flu vaccination coverage).

Discussion

The impact of flu on various populations has been a topic of great interest. Multiple strategies have been developed in the fight against flu epidemics, the cornerstone of which is vaccination. A study in eleven European countries demonstrated that gender, age, presence of chronic illness, household income, household size, educational level, and population size of living residence contribute to differences in flu vaccination rates [56]. Many countries have declared flu vaccination a priority healthcare goal, as immunisation is cost-effective [57,58] and efficient [59] in preventing flu-associated morbidities. However, flu vaccination coverage has not yet reached the established goals.

In this context, the COVID-19 pandemic changed the strategic arrangements regarding plans for flu vaccination. Recent studies have postulated that flu vaccination is associated with lower SARS-CoV-2 seroprevalence, hospitalizations, intensive care unit admissions, and deaths from COVID-19 [60]. Indeed, COVID-19 has resulted in a more positive intention for flu vaccination globally [61]. However, significant hesitancy towards flu vaccination due to the perceptions and misinformation surrounding flu and vaccination still exists [28,61]. Kong et al., in their meta-analysis, examine the effects of COVID-19 on flu vaccination intention [61]. The latter study finds the increased intention to vaccinate against flu during COVID-19 globally, regardless of region, age, gender, and occupation. A significant predictor of flu vaccination intention and/or uptake is the historical vaccine acceptance; other factors include an individual's perception of flu severity and the vaccine's safety. The increased intention to vaccinate against flu during COVID-19 is an encouraging finding, which can help mitigate the negative effects of the increased prevalence of coinfections [62]. Reasons for and against flu vaccination for the 2020/2021 flu season can be classified into participants' perception of flu vaccination, including perceived efficacy of the vaccine, side effects, and fear of administration method, perception of flu severity and risks, and COVID-19 pandemic and logistical issues [19–22,26–31,34,36–43,61]. The primary motivator for vaccination was the perceived benefits of flu vaccination [27,31,37,38,41,42] in protecting themselves and others from flu [27,36,37,41]. However, someone was apprehensive about taking the vaccine because they did not believe in its efficacy [19,31,37,41,63,64], feared the side effects [31,37,38,41] or needles [38,64], worried about the cost [22], or believed that vaccinations are a strategy to profit pharmaceutical companies[64]. Gerussi et al. reported, "*Vulnerable groups are less hesitant to vaccinations, and their frequent access to the hospital environment may favour contact with physician information and sensibilization campaigns*"[28]. In addition,

Fig. 2. The smoothed functional Flu Vaccination coverage of the Italian regions using b-splines and six interior knots (setting up a basis system with a knot at every data point).

they find that the presence and the number of comorbidities positively influenced decision-making regarding flu shots but not regarding the SARS-CoV-2 vaccine, and the previous COVID-19 infection influenced the tendency towards flu vaccine. Moreover, hesitancy was lower in those who experienced critical COVID-19 illness than in those who experienced milder disease [28]. Domnich et al. combined two cross-sectional questionnaires on 2543 Italian adults (≥18 years) from 2020 and 2021 to compare the change in attitudes towards the flu vaccine[64]. There was a significant increase in the percentage of trust in vaccines from 2020 to 2021 (from 18.3 % to 25.6 %; $p < 0.001$) due to the COVID-19 pandemic, and more people agreed that flu vaccination should be mandatory, and fewer believed it was a "fraud" [64]. In the same way, other recent studies reported a similar finding, where intent to be vaccinated against the flu was reported to have increased during the COVID-19 pandemic [5,28,61,64]. Genovese et al. investigated in a multicentric

Table 2
Change over time (from 2010 to 2022) of the membership value for each Italian region to Group 1 (G1).

Regions	Membership G1 (2010–2019)	Membership G1 (2010–2020)	Δ (2010–2020 vs 2010–2019)	Membership G1 (2010–2021)	Δ (2010–2021 vs 2010–2020)	Membership G1 (2010–2022)	Δ (2010–2022 vs 2010–2021)
Abruzzo	0.78	0.77	**-0.01**	0.73	**-0.05**	0.69	**-0.03**
Aosta Valley	0.79	0.78	**-0.01**	0.76	**-0.02**	0.75	**-0.01**
Apulia	0.23	0.23	**0.00**	0.26	**0.02**	0.27	**0.02**
Basilicata	0.28	0.29	**0.02**	0.46	**0.16**	0.44	**-0.01**
Calabria	0.47	0.48	**0.01**	0.48	**0.00**	0.48	**0.00**
Campania	0.55	0.56	**0.02**	0.58	**0.02**	0.60	**0.02**
Emilia-Romagna	0.23	0.23	**0.00**	0.24	**0.01**	0.24	**0.00**
Friuli-Venezia Giulia	0.44	0.42	**-0.02**	0.40	**-0.02**	0.41	**0.01**
Latium	0.46	0.50	**0.04**	0.40	**-0.10**	0.38	**-0.02**
Liguria	0.20	0.20	**0.00**	0.28	**0.08**	0.29	**0.01**
Lombardy	0.73	0.72	**0.01**	0.72	**-0.01**	0.71	**-0.01**
Marche	0.40	0.40	**0.00**	0.35	**-0.05**	0.34	**-0.01**
Molise	0.24	0.24	**0.00**	0.31	**0.07**	0.34	**0.04**
Piedmont	0.76	0.76	**0.00**	0.73	**-0.02**	0.73	**0.00**
Sardinia	0.78	0.78	**0.00**	0.72	**-0.06**	0.71	**-0.01**
Sicily	0.65	0.62	**-0.03**	0.50	**-0.12**	0.46	**-0.04**
Trentino - South Tyrol	0.71	0.71	**0.00**	0.71	**0.00**	0.68	**-0.02**
Tuscany	0.24	0.24	**0.00**	0.26	**0.02**	0.27	**0.01**
Umbria	0.27	0.26	**0.01**	0.27	**0.01**	0.28	**0.01**
Veneto	0.48	0.51	**0.03**	0.55	**0.04**	0.60	**0.04**

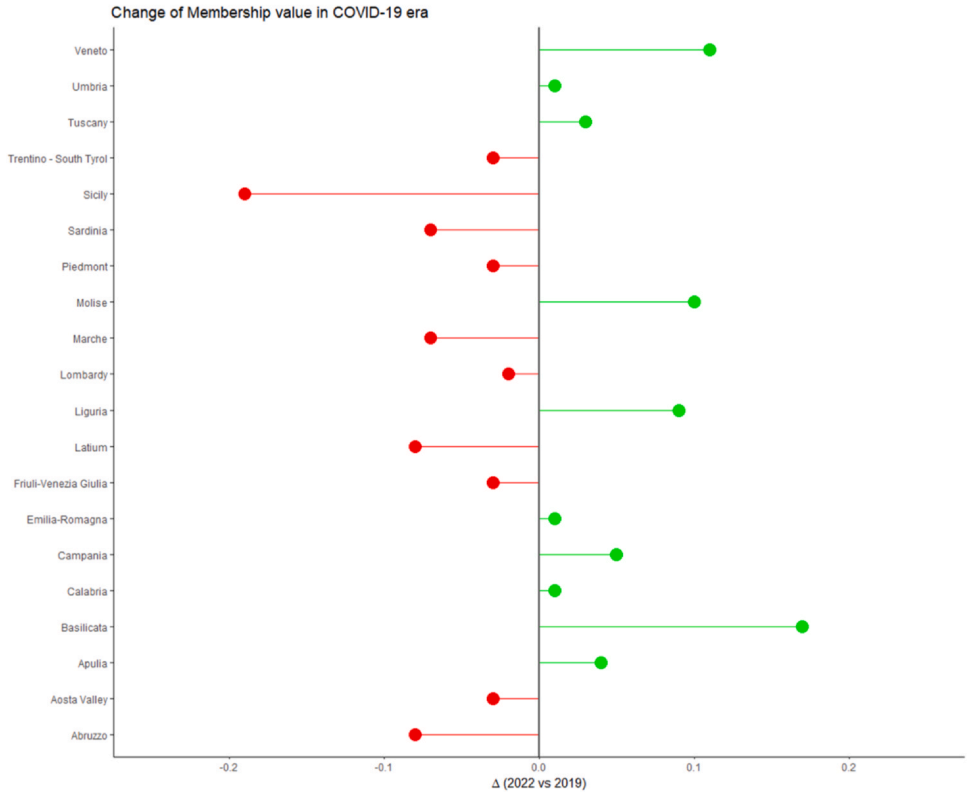

Fig. 3. Changes over time (2019 vs 2022) of the membership values for each Italian region to Group 1 (G1). Δ= differences.

Italian study the knowledge, attitude, and perception of flu and COVID-19 vaccination during the COVID-19 pandemic [65]. They highlight that a higher knowledge about SARS-CoV-2/COVID-19 and at least one flu vaccination during previous flu seasons were significantly associated with the intention to be vaccinated for flu. Thus, the COVID-19 pandemic has increased the acceptance rate in unvaccinated people of flu vaccinations. Del Riccio et al., 2021 reported the flu vaccine coverage rates across ten northern hemisphere countries (England, France, Israel, Italy, The Netherlands, Philippines, Poland, South Korea, Spain, United States) and Australia. Except for South Korea, all countries reported an increase in vaccine coverage rate from 2019/2020 to the 2020/2021 season [66]. The coverage rates pre-pandemic and during the pandemic reiterate the previously reported increase in trust and demand for flu vaccines due to COVID-19. There remains a scarcity of evidence investigating the cause of this, as multiple factors influence vaccination intent and are highly likely to vary depending on many situational factors [67–69]. Thus, as described in many studies, the COVID-19 pandemic was the impetus behind the increased intention to be vaccinated for flu, indicating that the pandemic may have fostered more positive health-seeking behaviour. Overall, the intention for flu vaccination (2020/2021) post COVID-19 was higher than in the 2019/2020 flu season across the studies reporting intention for the 2020/2021 season [22,29,38,41,64,64,65,70–78]. This increase in intention to vaccinate was observed in Asia, Europe, and North America. The increase in vaccination intention was significantly higher in Asia and Europe compared to North America [61]. However, some population surveys about flu vaccine uptake and the COVID-19 vaccine in Italy provide different results[28–31,79]. In 2020 in Italy, there were some population-based studies about accepting the COVID-19 and flu vaccines. An Italian representative survey based on 1055 Italians aged 15–85 was conducted and concluded that the attitude towards flu vaccination tended to be more favourable compared to the past. However, most (about 60 %) of the population, and almost 40 % of the subjects 55 and over, do not intend to accept flu vaccination for the following winter [29]. On the other hand, a representative cross-sectional survey on 2543 Italian subjects regarding the COVID-19 pandemic and the uptake of the 2020/21 flu vaccine highlights that participants (74.8 %) valued flu vaccination positively and declared that it should be mandatory. Thus, the COVID-19 pandemic may have positively influenced the vaccination propensity against 2020/21 seasonal flu [30]. Discordant results may be due to the sample collection and the lack of insight into the entire population. Italy shows strong regional heterogeneities due to economic, quality of life, socio-cultural, public policy and other disparities [53]. The differences between southern, northern and central Italy have always been known and must be considered. Regional disparities turn out to be a multidimensional phenomenon [80]. Fig. 3 reports the evidence for which regions' locations influences vaccination attitudes, emphasizing a spatial dependence when vaccination attitudes are to be examined. Indeed, it suffices to observe that Puglia, Basilicata, Calabria, Molise, and Campania, which are very close to each other and often adjacent, have a very similar variation. The same reasoning is valid in reverse for Piedmont, Lombardy, Valle d'Aosta and other northern regions. In light of our results, studies in the literature on the Italian territory that do not take into account the spatial heterogeneity may come to biased conclusions especially if they do not consider the differences among regions and thei past behaviours.

The literature shows that the population, as one might assume, is not vaccinating less for flu given the advent of COVID-19 and related vaccines. In contrast, COVID-19 seems to have increased the population's awareness of the importance of vaccination by providing an extra boost, particularly in Italy, by increasing the historically low vaccination coverage rate. However, at the national level, it is fundamental to spread positive communication in the field of vaccination to counteract the phenomenon of vaccine hesitancy, including the development of digital tools to facilitate progress towards empowerment and changes in citizens' behaviour [81].

Conclusions

The present study highlights that the COVID-19 era has resulted in a more high flu vaccination rate. Moreover, the regional level's improvement or worsening in flu vaccination is not affected by the historical gap and socio-cultural and economic differences prevailing among Italian regions.

Statements of ethical approval

Since this analysis was based on anonymous administrative data with no possibility of identifying subjects, Ethical Committee approval was not required in Italy.

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Declaration of Competing Interest

The authors declare that they have no conflicts of interest regarding the research conducted and the publication of this manuscript. This research received no grant from public, commercial, or not-for-profit funding agencies.

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