Master of Public Health

Master de Santé Publique

Attitudinal profiles of COVID-19 vaccination using the 7C model and their association with vaccination behaviour: A Latent Class Analysis in a large sample of French adults.

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List of acronyms

AIC: Akaike Information Criterion.

AUC-ROC: Area under the Receiver Operating Characteristic Curve

BIC: Bayesian Information Criterion.

CCA: Complete Case Analysis.

CI: Confidence Interval.

CM: Conditional Modes.

CNAM: Caisse Nationale d'Assurance Maladie

CNIL: Commission Nationale de l'Informatique et des Libertés.

DOM-TOM: overseas departments and territories.

GVIF: Generalised Variance Inflation Factors.

HPV: Human Papillomavirus Vaccine

ICC: Intraclass Correlation Coefficient.

KAP: Knowledge, Attitudes, and Practices

LCA: Latent Class Analysis.

LRT: Likelihood Ratio Test.

MCAR: Missing Completely at Random.

MCC: Matthews Correlation Coefficient.

MI: Motivational Interviewing.

OR: Odds ratio.

SD: Standard Deviation

VLMR: Vuong-Lo-Mendell-Rubin

Abstract

Background: Vaccination was crucial in mitigating the COVID-19 pandemic. Its success depended not only on logistics but also on widespread public trust in vaccines. However, in France, vaccination acceptance presented substantial heterogeneity, influenced by psychological, social, and demographic factors. This study aimed to identify different COVID-19 vaccination profiles (classes) among French adults using the 7C model of attitudinal antecedents (Confidence in vaccine, Low Complacency, Convenience, Calculation, Collective Responsibility, Social conformism, and Confidence in system) and to estimate the association between these profiles and vaccination behaviour.

Methods: Using a dataset of 47,980 adult participants from a French case-control study, a sample of 40,885 infected individuals with SARS-CoV-2 was randomly partitioned into a training (80%) and a validation (20%) set. Latent class analysis was conducted on the training set (n = 32,708) to derive attitudinal profiles based on responses to the questionnaire of the 7C model. A mixed-effects logistic regression model was used to assess the association between latent class membership and up to date COVID-19 vaccination status, adjusting for key sociodemographic characteristics and accounting for regional clustering.

Results: seven attitudinal profiles of COVID-19 vaccine were identified through the LCA analysis. After adjustment for sociodemographic covariates, all latent classes were statistically significantly associated with up to date vaccination status. The characterisation of these profiles highlights an overall favourable attitude towards perceived vaccine access across all classes. Class 1 and 7 were the classes with more unfavourable and undecided attitudes, including the diminished confidence in vaccines and confidence in the system, while class 5 and 6 were overall the most favourable towards COVID-19 vaccination.

Conclusions: The findings of this study provide insights into the nuanced attitudinal profiles towards COVID-19 vaccines, which could informe the development of targeted public health strategies and tailored communication to enhance vaccine uptake and epidemic preparedness.

Keywords: *COVID-19, Vaccination, Vaccine Hesitancy, Latent Class Analysis, Public Health.*

Profils attitudinaux vis-à-vis de la vaccination contre la COVID-19 selon le modèle des 7C et leur association avec le comportement vaccinal : une analyse en classes latentes sur un large échantillon d'adultes français.

Résumé

Contexte : La vaccination a joué un rôle crucial dans l'atténuation de la pandémie de COVID-19. Son succès ne dépendait pas uniquement des aspects logistiques, mais aussi de la confiance généralisée du public envers les vaccins. En France, toutefois, l'acceptation de la vaccination a été hétérogène. Elle a notamment été influencée par des facteurs psychologiques, sociaux et démographiques. La présente étude visait à identifier des profils (ou classes) vis-à-vis des vaccins contre la COVID-19 chez les adultes français, à l'aide du modèle des 7C des antécédents attitudinaux (Confiance dans le vaccin, Faible complaisance, Commodité, Calcul, Responsabilité collective, Conformisme social et Confiance dans le système), et à estimer l'association entre ces profils et le comportement vaccinal. **Méthodes :** À partir d'une base de données, comprenant 47 980 adultes et issue d'une étude cas-témoins française, un échantillon de 40 885 personnes infectées par le SARS-CoV-2 a été réparti aléatoirement en un ensemble d'apprentissage (80 %) et un ensemble de validation (20 %). Une analyse en classes latentes (ACL) a été réalisée sur l'ensemble d'apprentissage (n = 32 708) afin d'identifier des profils attitudinaux differents (à partir des réponses au questionnaire basé sur le modèle des 7C). Un modèle de régression logistique à effets mixtes a ensuite été utilisé pour évaluer l'association entre l'appartenance à une classe latente et le statut vaccinal à jour contre la COVID-19, en ajustant les principales caractéristiques sociodémographiques et en tenant compte de la variabilité régionale. **Résultats :** Sept profils d'attitudes vis-à-vis du vaccin contre la COVID-19 ont été identifiés grâce à l'analyse LCA. Après ajustement pour les covariables sociodémographiques, toutes les classes latentes étaient statistiquement significativement associées au statut vaccinal à jour. La caractérisation de ces profils met en évidence une attitude globalement favorable concernant l'accès perçu au vaccin dans l'ensemble des classes. Les classes 1 et 7 présentaient des attitudes plus défavorables ou indécises, notamment une confiance réduite envers les vaccins et envers le système, tandis que les classes 5 et 6 étaient globalement les plus favorables à la vaccination contre la COVID-19. **Conclusions :** Les résultats de cette étude apportent un éclairage sur les profils d'attitudes nuancés envers les vaccins contre la COVID-19, ce qui pourrait orienter le développement de stratégies de santé publique ciblées et de communications adaptées pour améliorer la couverture vaccinale et la préparation aux épidémies.

Mots-clés : *COVID-19, Vaccination, Hésitation vaccinale, Analyse en classes latentes, Santé publique.*

1. Introduction

1.1. Vaccines and the COVID-19 pandemic

Vaccines are considered one of the most cost-effective public health interventions, protecting individuals from potentially severe illnesses and enhancing herd protection (1). During the COVID-19 pandemic, vaccine uptake was essential for improving public health outcomes, significantly reducing morbidity, thereby decreasing emergency department visits and hospital admissions (2). Most importantly, COVID-19 vaccination played a key role in reducing mortality, preventing an estimated 14.4 million deaths across 185 countries and territories (3).

The effective deployment of COVID-19 vaccines relied not only on logistical factors, such as large-scale production, and equitable and fast distribution, but also on individual and societal factors, including confidence in vaccines and confidence in political leadership (4). Governments and other authorities promoted COVID-19 vaccination by launching public awareness and education campaigns. (5). However, there were significant differences in COVID-19 vaccine acceptance across populations (6). In some countries, vaccine acceptance was very high, with rates exceeding 80% in certain cases (6,7). Among European countries such as Germany, Italy and Spain, acceptance ranged between 64 and 69%, in contrast, France had an estimated acceptance rate of only 54% (6,7). To address the high proportion of individuals unwilling to get vaccinated and to help contain the COVID-19 pandemic, some governments implemented policies requiring proof of vaccination (8).

In France, the government required to hold a valid COVID-19 certificate, later replaced by a vaccination pass for accessing leisure and cultural venues (9). Following these measures, first-dose vaccine coverage among French adults increased up to 92.4%, but it later stagnated as most unvaccinated people decided to remain unvaccinated despite vaccine availability (9). As the case of France, global vaccine acceptance remained a significant challenge, with many people being hesitant to get vaccinated, less willing to receive booster doses, and sometimes more reluctant to vaccinate their children (5).

1.2. Vaccine acceptance

Vaccine acceptance is a complex, multi-dimensional process influenced by various contextual factors, including past vaccination experiences, collective perceptions of disease severity, interactions with the healthcare system, and trust in authorities (10). Over the past decade, researchers have introduced various concepts to better understand the factors influencing vaccine acceptance beyond sociodemographic characteristics (9). Early theoretical frameworks compared vaccine uptake to other health behaviours, emphasising the roles of health literacy, social norms, and self-efficacy in shaping individuals' decisions (9). Concepts such as vaccine hesitancy and readiness emerged to capture the scientific nuances of vaccination decision-making.

Vaccine hesitancy has been defined as the "delay in acceptance or refusal of vaccination despite availability of vaccination services" (11). Conversely, vaccination readiness refers to an individual's willingness and preparedness to receive a vaccine. It is a positively framed concept that encompasses various factors influencing a person's intention to get vaccinated (12). Readiness varies between individuals and can be influenced by interventions designed to enhance it, such as information campaigns, public discussions, and access to vaccines (12).

1.3. Models of vaccine readiness

Vaccine readiness has been analysed using various models that categorise the attitudinal antecedents, or components, that influence it. The initial model, known as the 3C model, included the following antecedents: *confidence* (the tendency to trust in the safety and effectiveness of vaccines, the system that delivers, and the incentives of policy-makers); *complacency* (the tendency to ignore vaccines because of a low perceived risk of vaccine-preventable diseases); and *convenience* (the ease of accessing and receiving vaccines, influenced by availability, affordability, geographic accessibility, and health literacy) (11).

The 3C model latter derived into the 5C model, which maintained *confidence* and *complacency*, while adding three more antecedents: *constraints* (structural or psychological barriers in daily life that make vaccination challenging or costly); *calculation* (the extent to which individuals assess costs and benefits of vaccination); and *collective responsibility* (the tendency to consider the protection of others when making vaccination decisions) (12,13).

1.3.1. The 7C model

Building upon the 5C model, during the COVID-19 pandemic, in parallel, Oudin Doglioni et al. (14) and Geiger et al. (12) developed the 7C model to include two more antecedents. In Germany and Denmark, Geiger et al. validated their extended 7C model on COVID-19 vaccines by adding *compliance* and *conspiracy. Compliance* referring to supporting collective monitoring and sanctioning of the unvaccinated, while *conspiracy* denoting a tendency to believe vaccine-related conspiracy theories and misinformation (12). At the same time, in

France, Oudin Doglioni et al. validated an extended 7C model on COVID-19 and HPV vaccines, showing its effectiveness in predicting vaccine acceptance across different populations (14). This extended 7C model proposed two alternative antecedents: *Confidence in the system* as a refined concept that frames the confidence given to vaccine recommendations, people who deliver them and adherence to conspiracy; and *social conformism* which focuses on the influence of family and friends (14). Furthermore, Moirangthem et al. confirmed that *confidence in systems* and *social conformism* were distinct antecedents of vaccination among French healthcare and welfare workers, which should be considered for vaccine promotion (15).

1.3.2. Applications of the 7C model

Araujo-Chaveron et al. applied the French 7C model to examine the evolving role of confidence in COVID-19 vaccine, identifying it as a key factor for booster uptake over time (16). Similarly, Lièvre et al. demonstrated, in a large cohort of French adults, that the 7C antecedents of vaccination explain not only COVID-19 vaccine intention but actual vaccine behaviour (9). It is worth noting that the 7C antecedents have been found to be different from personality traits, and their influence on vaccine behaviours is independent of them (17). Thus, suggesting that the 7C antecedents can be shaped through targeted information campaigns and vaccine promotion strategies (17).

In addition to studies on COVID-19, the 7C model has been used to develop other questionnaires such as the Knowledge, Attitudes, and Practices (KAP) survey, which examined changes in psychological antecedents of vaccination among French adolescent following exposure to HPV-vaccination-related interventions (18). In addition, the French 7C model has been recently applied by Cogordan et al. (19) to evaluate the impact of motivational interviewing (MI) training for health mediators working with disadvantaged populations, finding that MI interventions increased vaccine confidence and acceptance.

1.4. Targeted strategies to enhance vaccine acceptance

Understanding people’s attitudes toward vaccines is essential for developing effective public health strategies to improve vaccine acceptance and coverage. For instance, individuals who show low concern about the impact of COVID-19 are more likely to be uncertain about or refuse vaccination, indicating that those who perceive a lower risk from COVID-19 should be prioritised in targeted outreach efforts (20). This is particularly important in preparing for epidemics since long-term efforts are required to enhance positive attitudes towards vaccines before an outbreak occurs (17). Different interventions have proven effective in increasing vaccine readiness, including communication-based interventions (face-to-face communication), motivational interventions (motivational interviewing), and structural interventions (policies and educational campaigns) (6,19). Therefore, to optimise the impact of these interventions, it is crucial to understand and define the target populations more precisely.

As described above, in the context of the COVID-19 pandemics and other seasonal epidemics, large vaccine coverage is crucial to mitigate outbreaks and populations' vaccine acceptance plays a key role in achieving this. Despite the significant impact of COVID-19, vaccine acceptance in the French population remained low compared to other countries, highlighting the need for targeted public health interventions. Therefore, the present study has been carried out using data from a large sample of French adults that participated in the *ComCor* case–control study and responded to the "Cognitiv" questionnaire (9,21,22), its main aim is to identify attitudinal profiles among participants based on their responses to the 7C model, and to assess the association of these profiles with vaccine behaviour. To accomplish this, the objectives of the study are:

- To identify latent classes representing the 7C vaccine attitudinal profiles.

- To estimate the associations between 7C attitudinal profiles and up to date vaccination status by adjusting for key sociodemographic factors and accounting for regional clustering.

This study has been performed in the context of my internship at the *Institute Pasteur* within the Emerging Diseases Epidemiology Unit where several studies regarding COVID-19 vaccines have been previously published. During this time, I have also been involved as an external evaluator of the VaxAction project (*vax-action.eu*), which has allowed me to better understand the 7C model and its implications in public health. This thesis represents the work I have carried out during my internship, applying the knowledge and skills acquired throughout the Master of Public Health program.

2. Methods

2.1. Study design

This cross-sectional study was pre-registered for transparency (osf.io/6fc42). This study used data collected from French adults who participated in the *ComCor* case–control study (22,23) and then completed the "Cognitiv" questionnaire (9). The *ComCor* study provided sociodemographic data, SARS-CoV-2 infection and exposure history, and COVID-19 vaccination records. The "Cognitiv" questionnaire assessed attitudes toward COVID-19 vaccination using a shortened version of the 7C model (16) and assessed personality traits through other questions that were not relevant for our analyses.

2.2. Data Collection

Between February and June 2022, participants from the *ComCor* study were invited to complete the self-administered online "Cognitiv" questionnaire to assess cognitive factors and attitudes towards COVID-19 vaccination (6). This survey employed a shortened version of the original 7C model questionnaire, with each of the seven domains represented by a single item tailored to the 2022 vaccination context (16). Most responses were recorded using a 5-point Likert scale, except one that used a 3-point scale. Participants could decline to answer specific questions (Appendix 1). Invitations to complete the "Cognitiv" questionnaire were primarily issued to individuals who had recently been infected with SARS-CoV-2 (6).

2.3. Participants

The study population comprised 47,980 participants, of whom all SARS-CoV-2-infected individuals (cases) were included in the analyses performed in this thesis (n = 44,881; prior handling missing data). Cases were identified through the Caisse Nationale d'Assurance Maladie, the French national health insurance agency. To be eligible, individuals needed to have a registered email address with the agency (22).

2.4. Ethical considerations

The *ComCor* study received ethical approval from the Comité de Protection des Personnes Sud Ouest et Outre-Mer 1 on September 21, 2020, with additional approval for the "Cognitiv" questionnaire granted on February 1, 2022. CNIL authorised data processing on October 21, 2020. The anonymised dataset used in this study was encrypted and accessible only on-site.

2.5. Variable definitions

Sociodemographic characteristics included age (categorised into six ordinal levels from 18–28 up to 69+), sex (male, female), education level (initially categorised into thirteen levels, later for the regression model it was recategorised into four levels: "Inf. Baccalaureate, “Bac. or equivalent”, “Bac +2 to Bac +4”, and “Bac +5 to Bac +8"), country of birth (France or abroad), and profession (categorised into eight levels). Co-morbidities were recorded as a categorical variable (no comorbidity, one comorbidity, or two or more comorbidities). Region of residence was captured using a categorical variable including all 13 metropolitan French regions.

The outcome variable (*Up to date vaccination status*) assessing COVID-19 vaccination behaviour was the same variable used in the previous study performed by Lièvre et al. (9). This binary variable, representing vaccination status, aligned with French public health recommendations in effect during the study period (February - June 2022). *Up to date vaccination* status was coded as 0 ("not up to date") for individuals who had received either only one dose, or two vaccine doses and had no prior infection. It was coded as 1 ("up to date") for those who had received either three or more doses, or two doses plus a prior infection.

The 7C attitudinal antecedents of vaccination were assessed using single items for each domain, with responses on ordinal scales (9):

- *Confidence in vaccine (originally “Lack of confidence in vaccine”):* assessed fear of severe vaccine side effects (5-point scale: 1 = completely disagree to 5 = completely agree; higher scores indicated lower confidence before being transformed).
- *Low complacency:* assessed fear of severe illness from COVID-19 (5-point scale: 1 = completely disagree to 5 = completely agree)
- *Convenience (originally “Inconvenience”):* evaluated the perceived difficulty in obtaining a vaccination appointment (5-point scale: 1 = completely disagree to 5 = completely agree; higher scores indicated lower confidence before being transformed).
- *Calculation:* measured individual’s perceived benefit–risk balance of COVID-19 vaccination (5-point scale: 1 = completely disagree to 5 = completely agree).
- *Collective responsibility*: assessed the extent to which participants viewed vaccination as a social duty (5-point scale: 1 = completely disagree to 5 = completely agree).
- *Social conformism:* measured the influence of peer and family opinions about vaccination, (5-point scale: 1 = very sceptical to 5 = very supportive).

- *Confidence in system:* evaluated the influence of government encouragement on an individual's vaccination decision, originally measured in a 3-point scale, rescaled to a 5-point scale (1 = completely dissuades you; 5 = completely encourages you).

2.6. Data Preparation

2.6.1. Recodification

Variables not relevant to the aims of the analysis were removed from the original dataset. Variables retained for analysis were recoded, factorised, and transformed as appropriate. 7C antecedents were recoded to align with the same scale direction to ensure consistency and improve interpretability. Interpolation mapping was applied to convert the original three-point response scale (1–3) into a five-point scale (1–5), allowing for greater analytical granularity. Responses of "do not wish to respond" were treated as missing data.

2.6.2. Missing data

We calculated the percentage of missing data in the study sample and MCAR test was performed to assess if values were missing at random. Little's MCAR test was significant ($p < 0.05$), meaning that missing values do not occur randomly. However, the percentage of missing data was <10% for all variables (Appendix 2). Thus, we conducted a complete case analysis (CCA) to exclude participants with missing data, we included a *final sample of 40,885* individuals.

2.6.3. Splitting technique

Although not assessed in this thesis, the full study includes a third objective focused on evaluating the performance of the multilevel logistic regression model in predicting up to date vaccination status using a validation dataset. To support this objective, the dataset used in this thesis was randomly partitioned using a 80/20 train-test split (23). The training set included 80% of the data (n = 32,708), and the validation set included the remaining 20% (n = 8,807), using a fixed random seed *"set.seed(123)"* to ensure reproducibility. The training set was used to perform the latent class analysis and the mixed-effects logistic regression analyses in this thesis.

2.7. Latent Class Analysis (LCA)

LCA is a data reduction technique that identifies hidden subgroups within a dataset by estimating class membership probabilities based on observed response patterns (24, 25). It uses maximum likelihood estimation to model these probabilities, allowing for the classification of individuals into latent classes (also known as profiles), while accounting for complex and inconsistent response patterns (24). Each individual is assigned to the class with the highest posterior probability (ranging from 0 to 1), based on the model and observed data (24).

LCA relies on two key assumptions: (1) each latent class is internally homogeneous, meaning that individuals within a class are similar in their responses; and (2) local independence, assuming that observed variables are uncorrelated within each class (24). Local independence was tested by examining residual correlations and bivariate residuals (Appendix 3).

2.7.1. Class assignment

Models were first estimated with three latent classes ($k = 3$), and the number of classes was gradually increased up to 12, until convergence was achieved (when additional iterations no longer changed the parameter estimates). To ensure model stability, twenty repetitions were run for each class number. We assigned participants to the latent class for which they had the highest posterior probability of membership. If a participant had equal probabilities for multiple classes, we assigned them randomly to one of those classes.

To assess the reliability of class assignments, we calculated the difference between the highest and second-highest posterior probabilities. This measure was used to evaluate how accurately each participant was classified. A threshold of 0.1 (10%) was applied to distinguish between "confident" (difference ≥ 0.1) and "ambiguous" (difference < 0.1) classifications. We calculated the summary statistics, including counts, percentages, and probability gaps, for each class to examine how assignment certainty varied across classes (Appendix 4). Additionally, class prevalence (the sample proportion assigned to each class) was calculated.

2.7.2. Model Selection

The model selection process for this LCA was guided by different fit indices and the epidemiological interpretability of classes. Fit indicators included the Bayesian Information Criterion (BIC), Akaike Information Criterion (AIC), Chi-Square statistics, and entropy. When choosing the optimal number of classes, it is ideal to minimise BIC and AIC while ensuring that entropy remains as close to 1 as possible to indicate low classification uncertainty (25). It is also important to ensure that the class prevalence is high enough to include relevant and informative classes (26). Additionally, we performed the Vuong-Lo-Mendell-Rubin (VLMR) test to compare models with different numbers of latent classes. For this comparison, log-likelihood values were extracted for each model, and a likelihood ratio test (LRT) was conducted. A significant p-value from the VLMR test suggests that adding a class significantly improves the model fit (25). While statistical criteria were considered essential for selecting the optimal number of latent classes, the final decision also considered epidemiological relevance.

2.8. Mixed-effects logistic regression

An adjusted mixed-effects logistic regression was performed to estimate the associations between 7C class membership and up to date vaccination status while controlling for age, sex, education level, profession, country of birth and comorbidity (Appendix 5). The mixed-effects model included both, fixed effects (predictor and sociodemographic variables) and random effects (geographic region). Given the clustering of participants by region of residence across the 13 French regions, a random intercept for geographic region was incorporated into the model to account for between-region variability.

To assess the impact of covariate adjustment and identify potential confounding factors, the mixed-effects logistic regression model was compared to an unadjusted model to better understand the true effect of class membership. A nested model comparison was also performed between the fixed-effects and mixed-effects models to assess whether accounting for regional clustering significantly improved model fit. To quantify the proportion of variance in up to date vaccination status attributed to regional differences, we calculated the Intraclass Correlation Coefficient (ICC), which represents the ratio of between-group variance to total variance, providing insight into the extent of clustering effects (27). To assess the stability and reliability of the model and potential multicollinearity, the condition number of the Hessian and generalised variance inflation factors (GVIF) were calculated. Conditional modes were also obtained to show how each regions' baseline outcome deviates from the overall intercept after accounting for all model fixed effects.

2.9. Software and statistical packages

All statistical analyses were conducted in R software (version 4.3.3), using the *poLCA* package for LCA, and *lme4* for multilevel logistic regression. Data manipulation and visualization were performed with the *dplyr* and *ggplot2* packages, respectively.

3. Results

3.1. Descriptive characteristics of the study population

A total of 47,980 participants were included in this study (Table 1), in which 72% were women and 28% men. Nearly half of the participants (48%) were between 39 and 58 years old and the other half distributed between the younger and older groups. Among all participants, 7% reported being born outside of France. The distribution of participants by region of residence closely reflected that of the general French population (28), with the highest proportions living in Île-de-France (17%) and Auvergne-Rhône-Alpes (12%), and the lowest in the overseas departments and territories (DOM-TOM) (1.1%). In terms of profession, most respondents were senior executives (31%), followed by retirees (21%), while around 5% were self-employed and manual workers. Additionally, the population was roughly split between those with up to secondary education and those with at least a bachelor's degree. Approximately 25% of participants reported having at least one comorbidity and 94% reported having been infected. Vaccination coverage was high, with 95% being vaccinated and 89% having an up to date vaccination status. However, there was still a 5% of the participants who did not receive any vaccine, 5% who were not up to date with vaccination, and 5% whose up to date vaccination status was unknown.

Table 1. Description of the study population.

Characteristic	**N = 47,980**[1]
Sex	
Male	13,636 (28.4%)
Female	34,344 (71.6%)
Age	
18–28	3,042 (6.3%)
29–38	8,165 (17.0%)
39–48	11,663 (24.3%)
49–58	11,677 (24.3%)
59–68	8,570 (17.9%)
69+	4,863 (10.1%)
Country of birth	
France	44,647 (93.1%)
Abroad	3,209 (6.7%)
Do not know	4 (0.01%)
Prefer not to say	120 (0.3%)
Region	
Île-de-France	8,116 (16.9%)
Centre-Val de Loire	1,968 (4.1%)
Bourgogne-Franche-Comté	2,116 (4.4%)
Normandy	2,322 (4.8%)
Hauts-de-France	4,086 (8.5%)
Grand Est	4,758 (9.9%)
Pays de la Loire	2,644 (5.5%)
Brittany	3,039 (6.3%)
Nouvelle-Aquitaine	4,237 (8.8%)
Occitanie	4,605 (9.6%)
Auvergne-Rhône-Alpes	5,870 (12.2%)
Provence-Alpes-Côte d'Azur + Corsica	3,706 (7.7%)
DOM-TOM	513 (1.1%)
Profession	
Farmers	23 (0.01%)
Self-employed	1,055 (2.2%)
Senior executives	15,000 (31.3%)
Intermediate professions	10,053 (21.0%)
Employees	7,569 (15.8%)
Manual workers	1,318 (2.7%)
Retirees	9,910 (20.7%)
Inactive	3,052 (6.4%)
Education	
No school or left before finishing primary	26 (0.1%)
No diploma, stopped after primary or before end of middle school	138 (0.3%)

No diploma, schooled until or beyond middle school	426 (0.9%)
Primary School Certificate (CEP)	224 (0.5%)
Middle School Certificate (BEPC, DNB)	1,020 (2.1%)
CAP/BEP or equivalent vocational diploma	4,473 (9.3%)
High School Diploma (general or technical)	5,706 (11.9%)
Higher certs (law capacity, DAEU, ESEU)	318 (0.7%)
Professional Bac or equivalent vocational diploma	2,272 (4.7%)
2-year college degree (BTS, DUT, etc.)	8,733 (18.2%)
Bachelor's degree or equivalent (Bac+3/+4)	10,572 (22.0%)
Master's degree, Grandes Écoles, or PhD (health)	12,763 (26.6%)
PhD (non-health)	1,309 (2.7%)
Comorbidities	
No comorbidity	36,157 (75.4%)
One comorbidity	9,719 (20.3%)
Two or more comorbidities	1,791 (3.7%)
Prefer not to say	313 (0.7%)
Infection status	
Infected (Cases)	44,881 (93.5%)
Non-infected (Controls)	3,099 (6.5%)
Vaccine status	
Not vaccinated	2,430 (5.1%)
Vaccinated	45,370 (94.5%)
Not answered	180 (0.4%)
Up to date vaccination status	
Not up to date	2,536 (5.3%)
Up to date	42,834 (89.3%)
Not answered	2,610 (5.4%)

[1]n (%)

3.2. LCA analysis

3.2.1. Latent class membership selection

According to BIC, AIC and Chi^2, class 12 had the lowest metrics (500064.3, 497352.6 and 47501.8, respectively), showing a better model fit, while class 2 had the highest entropy (0.81), which gradually decreased to 0.69 by class 7, and then remained relatively stable through to class 12. Regarding the VLMR test, all p-values were extremely small, including the highest number of classes comparison, which was 11 vs 12 (p-value: 1.38×10^{-5}), meaning that the VLMR test did not suggest a clear “optimal” number of classes, as each additional class significantly improved model fit (Table 2).

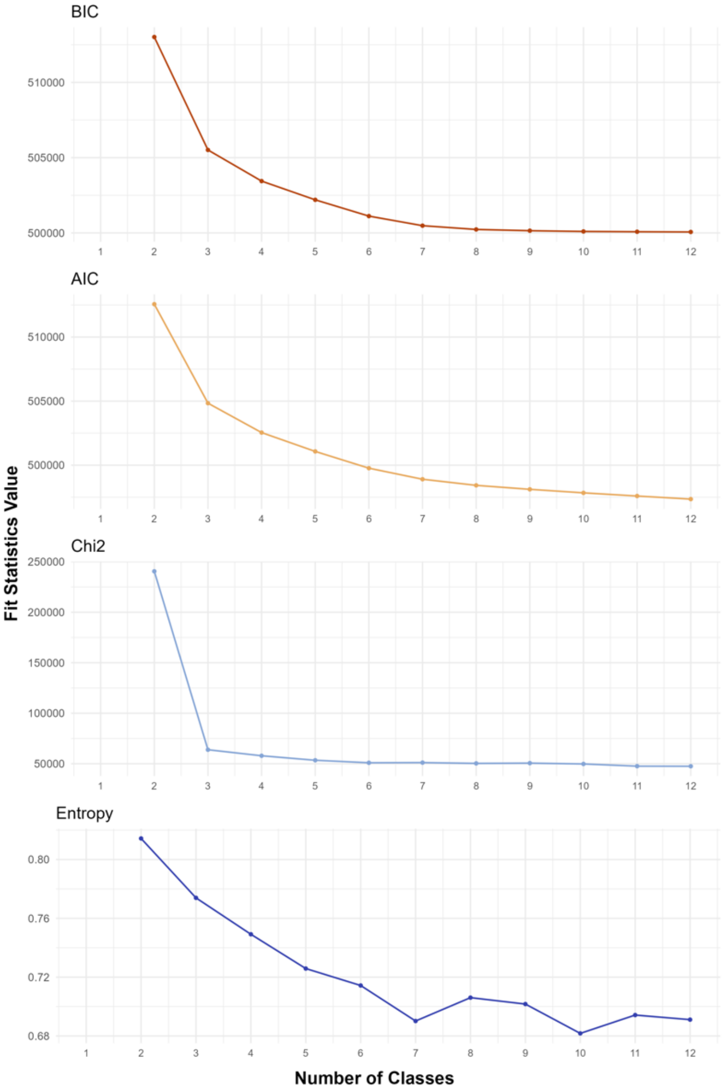
Table 2. Results from fit statistics and VLMR test for latent class selection.

Fit statistics					VLMR test		
Class	**BIC**	**AIC**	**Chi2**	**Entropy**	**Comparison**	**LRT statistic***	**p-value**
2	513011.8	512566.8	240511.6	0.81	2 vs 3	2233.2	0
3	505511.6	504840.0	63847.6	0.77	3 vs 4	581.3	4.86×10^{-104}
4	503442.9	502544.6	57883.7	0.75	4 vs 5	445.1	4.99×10^{-76}
5	502199.0	501074.1	53429.2	0.73	5 vs 6	278.3	1.54×10^{-42}
6	501118.0	499766.4	50939.3	0.71	6 vs 7	231.1	2.25×10^{-33}
7	500481.8	498903.4	51106.2	**0.69**	7 vs 8	153.9	5.88×10^{-19}
8	500231.3	498426.3	50336.0	**0.71**	8 vs 9	112.9	7.65×10^{-12}
9	500148.1	498116.4	50589.9	**0.70**	9 vs 10	89.8	3.84×10^{-8}
10	500098.3	497840.0	49771.8	**0.68**	10 vs 11	114.1	4.80×10^{-12}
11	500078.6	497593.6	47583.2	**0.69**	11 vs 12	72.5	1.38×10^{-5}
12	**500064.3**	**497352.6**	**47501.8**	**0.69**	LRT: Likelihood ratio test; ** Degrees of freedom: 29*		

As observed from the results shown in Table 2, statistically the model fit was better at 12 classes according to the BIC, AIC, Chi^2 and VLMR test. However, entropy dropped to 0.69 at seven classes and stabilised, suggesting that additional classes beyond seven did not offer better separation (Figure 1). Additionally, entropy at seven classes was still within the acceptable range (> 0.6) (29,30).

At the same time, adding more classes may lead to overfitting and less interpretable clusters as models with too many classes become harder to use in a meaningful way (29,30). Therefore, the best balance between statistical fitness and epidemiological interpretability was the 7-class model, which was the model we chose for this study. Additionally, the 7-class model showed an adequate class prevalence, with most classes having at least 5% of the sample (Table 5). The exception was Class 1 with a prevalence of 3.5% (1,149 observations), which was still a substantial number suitable for theoretical interpretation (30).

Figure 1. Visual description of fit statistics showing each measure corresponding to the number of classes obtained through the LCA.



3.3. Mixed-effects logistic regression

Once the number of classes was determined, fixed-effects and mixed-effects models were compared to assess whether accounting for regional variability as a random effect significantly improved model fit (Table 3). The mixed-effects model showed a higher log-likelihood (-5341.2 vs. -5347.8), lower AIC (10736.31 vs. 10747.56), and lower BIC (10962.94 vs. 10965.79) compared to the fixed-effects model. Additionally, the likelihood ratio test (LRT: 13.25, $p < 0.001$) confirmed that the mixed-effects model provides a significantly better fit. Based on these results, the mixed-effects model was selected to further examine heterogeneity in up to date vaccination status, accounting for regional differences captured in the data.

Table 3. Comparing models with and without regional random effects using LogLik, AIC, BIC, and LRT.

Model	LogLik	AIC	BIC	LRT	p-value
Fixed effects	-5347.8	10747.56	10965.79	–	–
Mixed effects	-5341.2	10736.31	10962.94	13.25	< 0.001

LogLik: Log-Likelihood; LRT: Likelihood ratio test.

Fixed Model equation: Up to date vaccination status ~ Class 1 + Class 2 + Class 3 + Class 4 + Class 6 + Class 7 + Sex + Age + Professions + Education + Country of birth + Comorbidities

Mixed Model equation: Up to date vaccination status ~ Class 1 + Class 2 + Class 3 + Class 4 + Class 6 + Class 7 +Sex + Age + Professions + Education + Country of birth + Comorbidities + (1 | Region)

The mixed-effects model was also compared to an unadjusted model to identify any confounding factor and understand the real effect of class membership (Table 4). When comparing the odds ratios and confidence intervals for class membership, they were nearly identical in both models, meaning that the association between class and up to date vaccination status was not substantially confounded by sex, age, profession, education, country of birth, or comorbidities. In both models, class 5 was used as the reference since it was the class with the highest proportion of observations. In the adjusted model, participants in all classes were significantly less likely to have up to date vaccination status compared to class 5 (Table 4). The odds ratios ranged from 0.01 in class 1 to 0.51 in class 6. Class 1 (OR: 0.01; 95% CI: 0.01 – 0.02) and class 7 (OR: 0.03; 95% CI: 0.03 – 0.04) were the least likely to be up to date with vaccination compared to class 5.

In addition, females had 28% higher odds of being up to date with vaccination than males, and those aged 29–38 had 26% lower odds than the 18–28 age reference group. Being born abroad was associated with 31% lower odds of being up to date with vaccination compared to being born in France. Individuals with comorbidities had higher odds of being up to date with vaccination, in particular those with two or more conditions (OR = 1.55; 95% CI: 1.10-2.20). No statistically significant associations were found for profession or education levels.

Regional differences had minimal impact, with an ICC of 0.01, indicating that only 1% of the variance in vaccination status was due to region of residence. Model fit statistics supported this, with a marginal R^2 of 0.327 and a conditional R^2 of 0.331, showing only a 0.4% increase when accounting for regional effects. Further observations on the effect of region of residence using conditional modes and results on the reliability of the mixed-effects model, are presented in Appendices 6 and 7, respectively.

Table 4. Unadjusted and adjusted association between 7C class memberships and up to date vaccination status. Mixed-effects model includes a fixed adjustment of sex, age, professions, education, country of birth and comorbidity; and random effects for region of residence (n = 32,708).

Covariates	Unadjusted model		Adjusted mixed effects model	
	Odds Ratio	95% Confidence Intervals	Odds Ratio	95% Confidence Intervals
Class membership				
Class 1	0.01	0.01 – 0.02*	0.01	0.01 – 0.02***
Class 2	0.15	0.11 – 0.20*	0.15	0.11 – 0.20***
Class 3	0.16	0.12 – 0.21*	0.16	0.12 – 0.22***
Class 4	0.17	0.13 – 0.22*	0.17	0.13 – 0.22***
Class 5 [Ref]	1.00	–	1.00	–
Class 6	0.51	0.38 – 0.68*	0.51	0.38 – 0.67***
Class 7	0.03	0.03 – 0.04*	0.03	0.03 – 0.04***
Sex				
Male [Ref]			1.00	–
Female			1.28	1.13 – 1.46***
Age				
18–28 years [Ref]			1.00	–
29–38 years			0.74	0.60 – 0.92**
39–48 years			0.96	0.78 – 1.19
49–58 years			1.06	0.85 – 1.32
59–68 years			0.95	0.72 – 1.26
69+ years			1.54	1.00 – 2.3

Professions				
Farmers [Ref]			1.00	–
Self-employed			1.32	0.13 – 13.47
Senior executives			2.19	0.22 – 22.06
Intermediate professions			2.49	0.25 – 25.01
Employees			1.85	0.18 – 18.58
Manual workers			1.20	0.12 – 12.13
Retirees			2.40	0.24 – 24.44
Inactive			1.57	0.16 –15.87
Education				
Inf. Baccalaureate [Ref]			1.00	–
Bac. or equivalent			0.95	0.80 – 1.14
Bac +2 to Bac +4			0.90	0.76 – 1.07
Bac +5 to Bac +8			0.85	0.69 – 1.04
Country of birth				
France [Ref]			1.00	–
Abroad			0.69	0.57 – 0.84***
Comorbidities				
No comorbidity [Ref]			1.00	–
One Comorbidity			1.20	1.04 – 1.39**
Two or more Comorbidities			1.55	1.10 – 2.20**
Random Effects			**Model fit**	
Region of residence (13 regions)				
Random intercept variance (τ_{00}, Region)		0.02	**Marginal R^2**	0.327
Standard Deviation (SD)		0.14	**Conditional R^2**	0.331

Residual variance (σ^2)	3.29	**Conditional number of Hessian**	11022.48
ICC (Intraclass Correlation Coefficient)	0.01		

Unadjusted model equation: up to date vaccination status ~ Class 1 + Class 2 + Class 3 + Class 4 + Class 6 + Class 7;

Adjusted mixed effects model equation: up to date vaccination status~ Class 1 + Class 2 + Class 3 + Class 4 + Class 6 + Class 7 +Sex + Age + Professions + Education + Country of birth + Comorbidities + (1 | Region);

* p-value < 0.05 ** p<0.01 *** p<0.001

3.4. Characterisation of selected latent classes

3.4.1. Graphical characterisation of latent classes

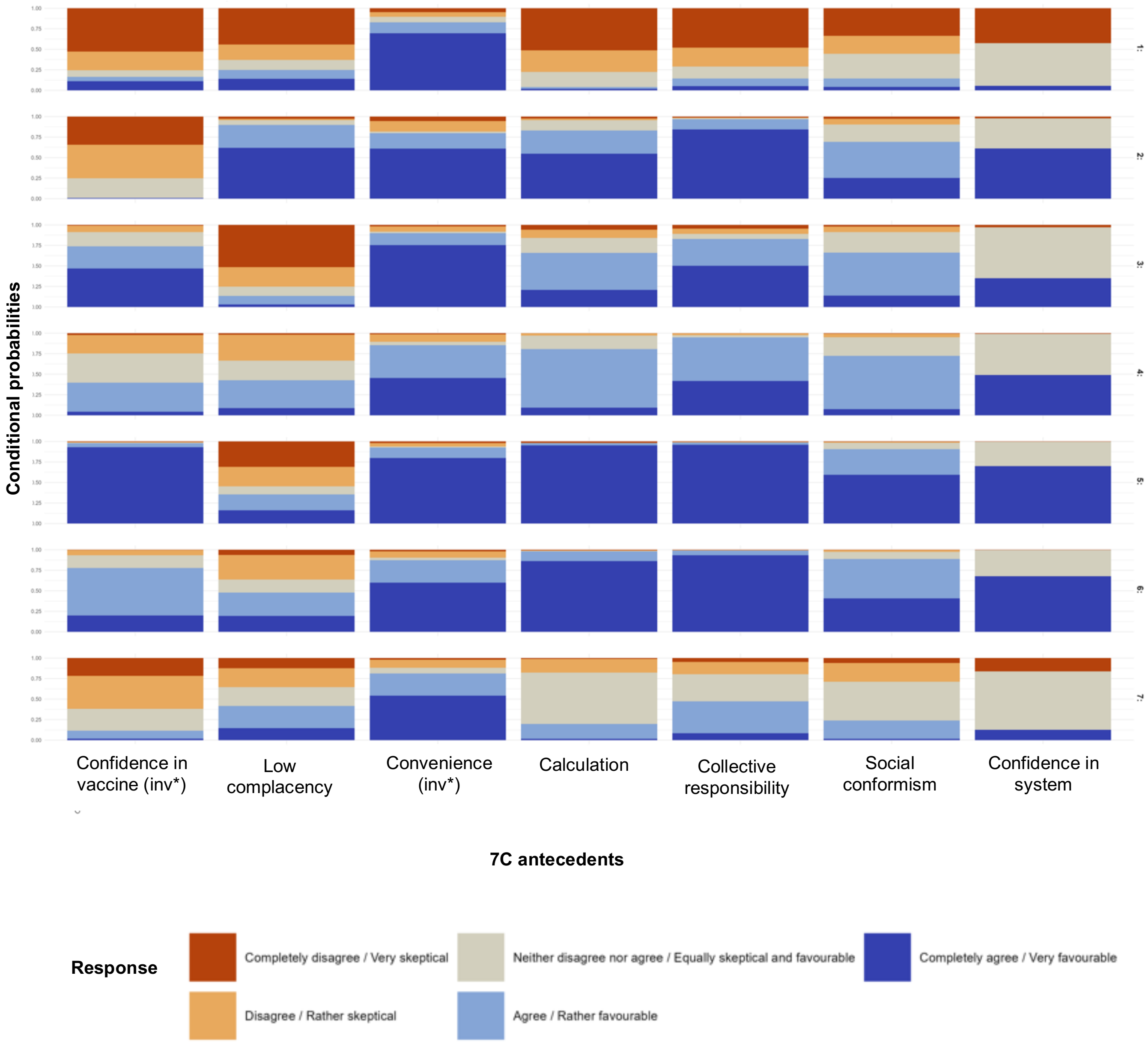
As observed in Figure 3, substantial differences were observed among the majority of classes for most antecedents, except for *convenience*, for which all classes had homogeneously favourable attitudes. Class 1 demonstrated a high probability of unfavourable or undecided responses for six out of the seven antecedents. Class 7 remained mainly undecided, with most 7C antecedents remaining neutral and some others also having a larger unfavourable (*confidence in vaccine*) or favourable (*collective responsibility*) responses. In contrast, class 5 and 6 were dominated by favourable attitudes across most antecedents, with the main difference that class 5 had more favourable responses for *confidence* in vaccines and more unfavourable responses in *low complacency* than class 6.

Intermediate classes (Classes 2–4) showed more heterogeneous responses, leaning more towards a favourable attitude. Except for *confidence in system*, which was divided between a large undecided attitude and a partly favourable attitude for all these classes. Furthermore, class 2 showed mainly agreement with most 7C antecedents, except with *confidence in vaccines*. This was also the only class that had a large favourable attitude for *low complacency*. Class 3 and 4 showed mainly favourable attitudes towards *convenience, calculation, collective responsibility, and social conformism*. Class 3 showed a larger unfavourable attitude with *low complacency* and favourable attitude with *confidence in vaccines* compared to class 4, which appeared to be more undecided and unfavourable for both antecedents.

3.4.2. Class description

As shown in Table 5, classes 5 and 6 represent the largest segments of the sample, comprising 28.0% and 27.8%, respectively. They are followed by class 4 (16.4%), and the smallest groups being class 1 (3.5%), class 2 (6.9%), and class 3 (6.6%). Regarding the sociodemographic characteristics, females are the majority across all classes, mainly in class 1 and 7 (81.3% and 82.7%). Among all classes, there is also a larger proportion of males in class 5 and 6 (37.6% and 31.0%). Age is overall balanced across classes, though some patterns can be identified. Classes 1, 3 and 7 have more younger participants aged 18–38 (11.9%, 9.3%, 8.5%); whereas classes 5 and 6 have the highest proportion of individuals aged 69 or above (15.1% and 12%).

Figure 3. Visualisation of the 7 latent classes and their corresponding conditional probabilities of responses in relation to the 7C antecedents.



** Inv. refers to "inverted" meaning that the variables were inverted by recodifying them as indicated in the methods section. Confidence in vaccine was originally "Lack of confidence in vaccine", and Convenience was originally "Inconvenience".*

Note on how to interpret the graph: Figure 3 shows the conditional probabilities of item responses across the latent classes, illustrating the distinct attitudinal antecedents that characterise each class. Each row corresponds to a latent class (7 in total), and each column represents a 7C antecedent. Within each cell, the stacked bars indicate the probability of endorsing each possible response category, ranging from negative (red: "completely disagree/very sceptical", orange: "disagree/rather sceptical") to positive (light blue: "agree/rather favourable", blue: "completely agree/very favourable") and neutral responses (grey shades).

As observed in Table 5, most participants across all classes were born in France (over 92%), with minor variations. Slightly higher proportions of individuals born abroad were in class 2 and 5 (8.3% and 7.9%). Education level varied between classes. Classes 5 and 6 had higher proportions of highly educated participants (Bac +5 to +8: 40.6% and 36.4%), while the other classes had higher proportion of Bac +2 to +4 (~40-45%). Classes 7 and 1 had also large proportion in lower education levels (under Bac: 19.0% and 19.1%).

Occupational roles also differed across classes. Classes 5 and 6 were predominated by senior executives (38.1% and 37.7%) and retirees (28.2% and 24.5%). Classes 1 and 7 had more diverse professionals, with higher percentages of intermediate professions (27.6% and 27.2%) and employees (24.8% and 25.7%). In particular, class 1 had the lowest proportion of retirees (8.3%), the largest group of manual workers (5.3%) and inactive individuals (11.1%) among all classes. Regional distribution was similar as the one seen in the study population, with Île-de-France consistently showing the highest representation, while DOM-TOM having the lowest.

When examining comorbidities, most participants reported none, with the largest proportions found in class 1 (78,7%), class 3 (83.2%) and class 7 (78.1%). In contrast, class 2 had the highest shares of individuals reporting one (24.8%) and two or more comorbidities (5.8%), followed by class 5 and 6. Up to date vaccination status varied considerably across classes, Classes 5 and 6 had the highest rates of up to date vaccination status (99.2% and 98.5%). In contrast, class 1 had the highest proportion of participants not up to date with vaccination (37%), followed by class 7 (19.2%).

Table 5. Sociodemographic description by class.								
Variable	**Level**	**Class 1**	**Class 2**	**Class 3**	**Class 4**	**Class 5**	**Class 6**	**Class 7**
Total	32708 (100%)	1149 (3.5%)	2248 (6.9%)	2149 (6.6%)	5359 (16.4%)	9145 (28.0%)	9098 (27.8%)	3560 (10.9%)
Sex	Female	934(81.3%)	1730(77%)	1623(75.5%)	4158(77.6%)	5704(62.4%)	6277(69.0%)	2945(82.7%)
	Male	215(18.7%)	518(23%)	526(24.5%)	1201(22.4%)	3441(37.6%)	2821(31.0%)	615(17.3%)
Age	18–28 years	137(11.9%)	167(7.4%)	200(9.3%)	308(5.7%)	453(5.0%)	418(4.6%)	304(8.5%)
	29–38 years	317(27.6%)	376(16.7%)	415(19.3%)	918(17.1%)	1112(12.2%)	1316(14.5%)	835(23.5%)
	39–48 years	321(27.9%)	616(27.4%)	566(26.3%)	1473(27.5%)	1849(20.2%)	2140(23.5%)	1049(29.5%)
	49–58 years	230(20.0%)	597(26.6%)	513(23.9%)	1352(25.2%)	2347(25.7%)	2258(24.8%)	808(22.7%)
	59–68 years	98(8.5%)	319(14.2%)	334(15.5%)	916(17.1%)	2002(21.9%)	1876(20.6%)	422(11.9%)
	69+ years	46(4.0%)	173(7.7%)	121(5.6%)	392(7.3%)	1382(15.1%)	1090(12.0%)	142(4.0%)
Country of birth	Abroad	65(5.7%)	186(8.3%)	94(4.4%)	321(6.0%)	720(7.9%)	645(7.1%)	206(5.8%)
	France	1076(93.6%)	2058(91.5%)	2051(95.4%)	5023(93.7%)	8418(92.1%)	8439(92.8%)	3344(93.9%)
Education	Inf. Bac. *	219(19.1%)	391(17.4%)	276(12.8%)	721(13.5%)	801(8.8%)	855(9.4%)	675(19.0%)
	Bac. or equivalent	267(23.2%)	435(19.4%)	368(17.1%)	976(18.2%)	1160(12.7%)	1166(12.8%)	869(24.4%)
	Bac +2 to Bac +4	480(41.8%)	890(39.6%)	917(42.7%)	2383(44.5%)	3475(38%)	3762(41.3%)	1439(40.4%)
	Bac +5 to Bac +8	183(15.9%)	532(23.7%)	588(27.4%)	1279(23.9%)	3709(40.6%)	3315(36.4%)	577(16.2%)
Professions	Senior executives	234(20.4%)	632(28.1%)	694(32.3%)	1623(30.3%)	3487(38.1%)	3434(37.7%)	766(21.5%)
	Intermediate professions	317(27.6%)	486(21.6%)	567(26.4%)	1319(24.6%)	1515(16.6%)	1797(19.8%)	968(27.2%)
	Employees	285(24.8%)	486(21.6%)	365(17.0%)	958(17.9%)	814(8.9%)	950(10.4%)	915(25.7%)
	Inactive	128(11.1%)	181(8.1%)	135(6.3%)	258(4.8%)	444(4.9%)	424(4.7%)	297(8.3%)
	Retirees	95(8.3%)	350(15.6%)	275(12.8%)	947(17.7%)	2582(28.2%)	2227(24.5%)	361(10.1%)
	Manual workers	61(5.3%)	66(2.9%)	66(3.1%)	145(2.7%)	130(1.4%)	113(1.2%)	157(4.4%)
	Self-employed	28(2.4%)	46(2.0%)	47(2.2%)	109(2.0%)	169(1.8%)	151(1.7%)	95(2.7%)
	Farmers	1(0.1%)	1(0.01%)	0	0	4(0%)	2(0%)	1(0%)
Region	Île-de-France	148(12.9%)	358(15.9%)	291(13.5%)	844(15.7%)	1782(19.5%)	1650(18.1%)	416(11.7%)
	Auvergne-Rhône-Alpes	129(11.2%)	243(10.8%)	267(12.4%)	648(12.1%)	1168(12.8%)	1151(12.7%)	414(11.6%)
	Grand Est	129(11.2%)	246(10.9%)	226(10.5%)	540(10.1%)	863(9.4%)	866(9.5%)	400(11.2%)
	Provence-Alpes-Côte d’Azur + Corsica	123(10.7%)	146(6.5%)	181(8.4%)	378(7.1%)	680(7.4%)	610(6.7%)	310(8.7%)
	Hauts-de-France	122(10.6%)	246(10.9%)	185(8.6%)	481(9.0%)	678(7.4%)	742(8.2%)	356(10.0%)

	Occitanie	117(10.2%)	220(9.8%)	224(10.4%)	488(9.1%)	892(9.8%)	838(9.2%)	373(10.5%)
	Nouvelle-Aquitaine	91(7.9%)	189(8.4%)	190(8.8%)	486(9.1%)	819(9.0%)	754(8.3%)	329(9.2%)
	Normandy	66(5.7%)	115(5.1%)	92(4.3%)	275(5.1%)	401(4.4%)	457(5%)	181(5.1%)
	Brittany	60(5.2%)	137(6.1%)	147(6.8%)	383(7.1%)	551(6.0%)	629(6.9%)	213(6.0%)
	Pays de la Loire	50(4.4%)	121(5.4%)	116(5.4%)	312(5.8%)	502(5.5%)	562(6.2%)	182(5.1%)
	Bourgogne-Franche-Comté	48(4.2%)	90(4.0%)	124(5.8%)	254(4.7%)	379(4.1%)	369(4.1%)	175(4.9%)
	Centre-Val de Loire	40(3.5%)	94(4.2%)	83(3.9%)	221(4.1%)	373(4.1%)	391(4.3%)	153(4.3%)
	DOM-TOM	26(2.3%)	43(1.9%)	23(1.1%)	49(0.9%)	57(0.6%)	79(0.9%)	58(1.6%)
Comorbidities	No comorbidity	904(78.7%)	1559(69.4%)	1787(83.2%)	4149(77.4%)	6850(74.9%)	6738(74.1%)	2779(78.1%)
	One comorbidity	215(18.7%)	558(24.8%)	309(14.4%)	1033(19.3%)	1961(21.4%)	1989(21.9%)	662(18.6%)
	Two or more comorbidities	30(2.6%)	131(5.8%)	53(2.5%)	177(3.3%)	334(3.7%)	371(4.1%)	119(3.3%)
Up to date vaccination	Not up to date	425(37%)	111(4.9%)	102(4.7%)	235(4.4%)	71(0.8%)	137(1.5%)	682(19.2%)
	Up to date	724(63%)	2137(95.1%)	2047(95.3%)	5124(95.6%)	9074(99.2%)	8961(98.5%)	2878(80.8%)

*"Bac." refers to Baccalaureate, the academic degree given when completing secondary education in France.

4. Discussion

The present work involves a large study population of French adults who completed the "Cognitiv" questionnaire in 2022, and whose responses have been used for a further classification and understanding of behaviours towards COVID-19 vaccines. By using 80% of the study population (n = 32,708) for the LCA, a 7-class model was selected. The mixed-effects logistic regression showed that all 7C attitudinal classes were statistically significant predictors of up to date vaccination status. Compared to class 5, all other classes were less likely to have the outcome, with classes 1 and 7 showing the strongest differences, even after adjustment.

Considering that the seven classes identified through LCA may reflect heterogenous population subgroups, it is important to carefully examine them for their potential role in guiding tailored public health interventions. As seen from the graphical characterisation of the selected classes, class 1 and 7 shared a pattern of unfavourable or undecided attitudes in terms of *confidence in vaccine, calculation,* and *confidence in the system,* which match results from previous studies in the French population. On one hand, it has been shown that people lost confidence in the government's ability to manage the COVID-19 pandemic (31) and felt that government's attention was insufficient towards their needs (20). On the other hand, studies have shown that fear of serious adverse events or the belief that COVID-19 vaccines were developed too quickly, negatively influence people's attitudes toward vaccination (32–34). It has also been found that among the young French population, vaccine hesitancy is more common among women and individuals with lower levels of education (20,35). A trend seen in these classes, which include a large number of young women and individuals with lower education levels.

Although these two classes represent only 14.4% of the population, the patterns observed in each class can inform public health strategies to improve vaccine uptake by targeting these specific groups. Generally, individuals such as those in class 1, who represent only 3.5% of the sample and who are the most vaccine-hesitant group, tend to cope with perceived health risks by rejecting COVID-19 concerns, often through conspiracy beliefs and vaccine refusal (36). Public health strategies that promote vaccination in individuals from Class 1, may have limited success due to their likely deep-rooted rejection of vaccines (35,37). However, it has been proposed that by fostering trust in scientists, implementing public education campaigns, increasing communication about the collective benefits of herd immunity, and providing targeted economic support, it might be possible to reduce scepticism and promote greater adherence to health behaviours, especially during a pandemic (35,37). Additionally, it has been recognised that by providing a better understanding of adverse events, it might be possible to increase vaccine acceptance among hesitant groups (16,38). Therefore, all these strategies might be more effective for those individuals in Class 7, who are undecided, represent a larger share of the population (10.9%), and may be more receptive to vaccination when provided with additional information about vaccines (35,37).

Another important strategy targeting these classes should be the reduction of people's mistrust of vaccines when it is driven by political factors as they might overshadow mistrust due to adverse effects (31,39). For certain groups, the COVID-19 pandemic was politically motivated, with claims that governments acted to serve the commercial interests of pharmaceutical companies (39). This might be reflected in the lack of *confidence in the system*, which has been prominent in classes 1 and 7, but also present to a lesser extent in less hesitant groups (classes 2, 3, and 4), and even among the most vaccine-favourable groups (classes 5 and 6), though in smaller proportions. Therefore, gaining deeper insight into how distrust in the system contributes to vaccine hesitancy could help in designing more effective communication strategies to address it among different classes.

An interesting finding among the intermediate classes (2, 3, and 4) was that, although their responses generally leaned more towards a favourable attitude around vaccines, class 2 showed a large unfavourable attitude towards *confidence in vaccines* and higher attitudes of *low complacency*, meaning that a larger proportion of people indicated that they were afraid of COVID-19 severity. This may be linked to their health status, as this group had the highest proportion of individuals with comorbidities. These results are consistent with previous findings showing that individuals with pre-existing health conditions often express greater mistrust toward COVID-19 vaccines, primarily due to concerns about how vaccination may affect their underlying illnesses or cause adverse side effects (40–42). The opposite was observed in Class 3, where most individuals were favourable for *confidence in vaccine,* but showed larger unfavourable attitude towards low *complacency*. This may be due to the group having the highest proportion of individuals without comorbidities (83.2%); thus they may have fewer concerns about potential COVID-19 vaccine side effects as they might feel less vulnerable than class 2 individuals.

While various public health strategies can be tailored to the different 7C attitudinal profiles to reduce hesitancy and improve uptake as discussed above for the most unfavourable and intermediate classes, one approach that may be effective across all vaccine unfavourable and undecided profiles is Motivational Interviewing (MI). MI might be particularly useful for addressing concerns about vaccine side effects and emphasize the collective benefits of vaccination as it engages patients in respectful, empathetic conversations with health professionals that explore their concerns and motivations rather than confronting or persuading them to vaccinate (43,44). This method has already been incorporated in an effective way in other vaccination campaigns such as HPV and Hepatitis B vaccination (45–47). It would be interesting to further investigate whether the seven profiles derived from the LCA might assist healthcare professionals who use MI to reduce COVID-19 vaccine hesitancy, and whether this approach could be extended to vaccines for seasonal illnesses such as influenza or whooping caught.

4.1. Discussion on the methodological aspects of class selection

Determining the optimal number of classes is challenging, as it requires balancing statistical fit with epidemiological relevance and interpretability (29). While statistical criteria for class selection continue to evolve and are debated, a statistically optimal solution has limited value if it lacks theoretical meaning (26,29,30). In this study, although BIC, AIC, Chi², and the VLMR test indicated improved fit with additional classes, entropy decreased and stabilized around 0.69 from 7 to 12 classes. The 7-class model was selected for having the best balance between being statistically appropriate and epidemiologically interpretable, with all but one class exceeding 5% of the sample and the smallest class (3.5%, n = 1149) being sufficiently large for statistical analysis. Thus, we believed that this model maintains acceptable entropy (>0.6), avoids overfitting, and provides meaningful distinctions that can inform targeted public health strategies.

4.2. Study limitations

Although the study includes a large sample size, it does not fully represent the adult population in France as of 2022. This limitation arises from differences in recruitment methods as most respondents to the “Cognitiv” questionnaire were recently infected individuals recruited nationwide, while non-infected participants were selected from a panel maintained by a market and public opinion firm. Consequently, the sample more accurately represents the adult population infected with SARS-CoV-2 than the general French population. Moreover, factors such as voluntary participation, digital literacy, and computer access may have further affected the sample's representativeness as participants were only those who had access to a device due to the pandemic context.

The study’s cross-sectional nature also presents certain limitations, including the risk of reverse causality (e.g., vaccine uptake influencing attitudes), which is hard to determine as this questionnaire was applied only once in the study population. Temporality may also be a limitation, as the 7C antecedents were assessed after participants had received their first vaccine dose. However, since participants could still become up to date with their vaccination status, exposure and outcome were assessed at the same time. Furthermore, responses related to the 7C antecedents may change over time, depending on when the questionnaire is administered. For example, during a pandemic or epidemic versus a period of public health stability or a localised outbreak. As a result, the interpretation of the LCA is limited to the specific time point at which the data were collected.

Another limitation is the high intercorrelation among the 7C antecedents, which may influence the interpretability of the LCA. However, the final model was deemed epidemiologically meaningful while considering the statistical recommendations from model fitness, reinforcing the validity and usefulness of the identified profiles for subsequent analysis.

4.3. Study strengths and prospected analyses

Despite the described limitations, the study remains appropriate and valuable due to its large sample and rigorous analytical methods. The focus on individuals recently infected with SARS-CoV-2 provides important insights into vaccine attitudes within a key population segment, which in the case of COVID-19 was a large group. Additionally, the epidemiological relevance of the latent class analysis increases the practical value of the findings, since they may provide meaningful guidance for public health strategies targeting vaccine hesitancy. Moreover, they can be used to support further analysis to assess their predictive value for vaccination behaviour.

As previously outlined in the methodology of this thesis, a third analysis will be conducted to evaluate the performance of the multilevel logistic regression model in predicting up to date vaccination status. This evaluation will be carried out using the validation dataset and the subgroup of non-infected individuals (control group). Model performance will be assessed using the Matthews Correlation Coefficient, complemented by the Area Under the Receiver Operating Characteristic Curve (AUC-ROC). The results of this third analysis will offer additional insights that complement the thesis findings on vaccination-related behaviours according to class membership. This will help predict an individual’s likely vaccination behaviour based on their profile and support the design of targeted vaccination programs tailored to specific groups, as previously suggested through vaccination campaigns and motivational interviewing approaches.

5. Conclusions

In this study, we identified seven epidemiologically meaningful profiles among French adults based on the 7C attitudinal antecedents of COVID-19 vaccination. Although the sample primarily comprises individuals infected with SARS-CoV-2, the results offer valuable insights into the complex attitudinal profiles associated with vaccination behaviours. All seven classes were significantly associated with up to date vaccination status. Patterns of unfavourable or undecided attitudes regarding *confidence in vaccine and in the system* as well as favourable attitudes regarding *convenience* were observed among the different profiles. These findings may inform the development of tailored public health strategies that improve vaccine acceptance and uptake based on specific attitudinal profiles, thereby supporting future outbreak preparedness.

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7. Appendices

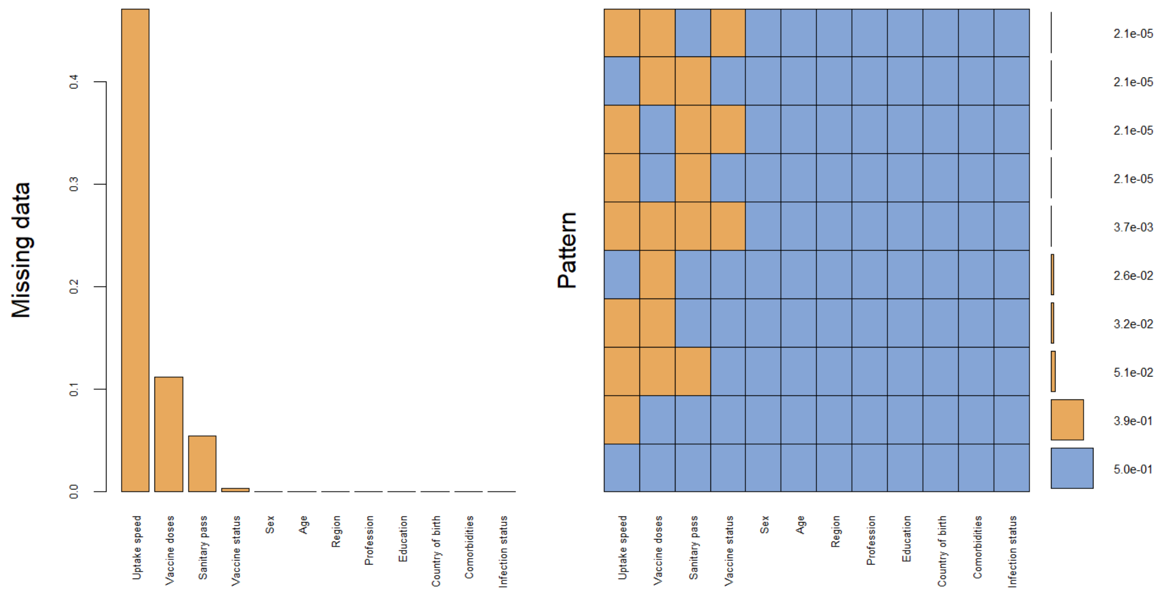
Appendix 1. Codebook of the dataset used from *ComCor* and Cognitiv questionnaires, indicating the recodification performed for this study.

Variable	Questions	Code	Labels	Recoded/Renamed
QCIBLE	Identification of the target	1	CIBLE A = CASES (Recruited by CNAM)	
		2	CIBLE B = CLOSE CONTACTS/RELATIVES (Invited by CAS)	
		3	CIBLE C = CONTROLS (Recruited by IPSOS)	
		4	CIBLE C = PERSONAL CAREGIVER WITNESS	
QSEXE	Respondent's sex	1	Man	
		2	Woman	
QAGE	Age group	1	18–28 years old	
		2	29–38 years old	
		3	39–48 years old	
		4	49–58 years old	
		5	59–68 years old	
		6	69 years old and above	
QREG	Regions	1	Île-de-France	
		2	Centre - Val de Loire	
		3	Bourgogne - Franche-Comté	
		4	Normandy	
		5	Hauts-de-France	
		6	Grand Est	
		7	Pays de la Loire	
		8	Brittany	
		9	Nouvelle-Aquitaine	
		10	Occitanie	
		11	Auvergne-Rhône-Alpes	
		12	Provence-Alpes-Côte d'Azur + Corsica	
R4	Recoded profession of the interviewee	1	Farmers	
		2	Self-employed professionals	
		3	Senior executives	
		4	Intermediate professions	
		5	Employees	
		6	Workers	
		7	Retired	
		8	Inactive	
QG16	What is the highest degree you have obtained?	1	You have never attended school or left before finishing primary school	Inf. Bac.*
		2	No diploma and left school at the end of primary or before finishing middle school	
		3	No diploma and schooling until the end of middle school or beyond	
		4	CEP (Primary School Certificate)	
		5	BEPC, elementary certificate, middle school certificate, DNB	
		6	CAP, BEP or equivalent level diploma	Bac. or equivalent
		7	General or technological Baccalaureate	
		8	Higher certificate, law qualification, DAEU, ESEU	
		9	Vocational Baccalaureate, professional certificate, technician diploma, or equivalent	
		10	BTS, DUT, Deug, Deust, health or social diploma at bac+2 level, or equivalent	Bac. +2 to +4
		11	Bachelor's degree, professional bachelor's, master's year 1, or equivalent bac+3/bac+4 level diploma	
		12	Master's, DEA, DESS, grande école diploma at bac+5 level, medical doctorate	Bac. +5 to +8
		13	PhD (excluding medical doctorate)	
QG18	In which country were you born?	1	In France	
		2	Abroad	
		3	You don't know	
		4	Prefer not to answer	
QG11_1	Do you suffer from any of the following illnesses?	1	Diabetes	Comorbidities variable
QG11_2		1	High blood pressure	
QG11_3		1	Angina / heart attack	
QG11_4		1	Chronic respiratory disease (chronic bronchitis, asthma, ...)	
QG11_5		1	None of these illnesses	
QG11_6		1	Prefer not to answer	
Comorbidities	New varible created from all individual comorbidities (QG11_1 to QG11_6)	0	No comorbidity	
		1	One comorbidity	
		2	Two or more comorbidities	
		3	Prefer not to say	
CA9B3 (Vaccine_doses)	How many COVID-19 vaccine injections have you received?	1	One injection	
		2	Two injections	
		3	Three injections	
		4	Four injections	
Vaccine_status	Is the person vaccinated?	0	Not vaccinated	
		1	Vaccinated	
Up-to-date_vaccination	Is the person up to date with the sanitary pass?	0	One or two doses without infection	Not up to date
		1	Two doses with infection, three doses or more	Up to date
Uptake_speed	Number of days passed to get vaccinated since elegibility		Continuous	
C3_1	I am afraid to develop a severe side effect after a COVID-19 vaccination. [*Lack of confidence in vaccine*]	1	Completely disagree	1 <=> 5, 2 <=> 4 Confidence in vaccine (inv)
		2	Disagree	
		3	Neither disagree nor agree	
		4	Agree	
		5	Completely agree	
		6	Does not wish to answer	
C3_2	I am afraid to develop a severe form of COVID-19. [*Low complacency*]	1	Completely disagree	
		2	Disagree	
		3	Neither disagree nor agree	
		4	Agree	
		5	Completely agree	
		6	Does not wish to answer	
C3_3	In practice, it is difficult for me to get an appointment to be vaccinated. [*Inconvenience*]	1	Completely disagree	1 <=> 5, 2 <=> 4 Convenience (inv)
		2	Disagree	
		3	Neither disagree nor agree	
		4	Agree	
		5	Completely agree	
		6	Does not wish to answer	
C3_4	I think COVID-19 vaccination has more benefits than risks for me. [*Calculation*]	1	Completely disagree	
		2	Disagree	
		3	Neither disagree nor agree	
		4	Agree	
		5	Completely agree	
		6	Does not wish to answer	
C3_5	Getting vaccinated is also a collective action to stop the crisis associated with the epidemic. [*Collective responsibility*]	1	Completely disagree	
		2	Disagree	
		3	Neither disagree nor agree	
		4	Agree	
		5	Completely agree	
		6	Does not wish to answer	
C4	Among your family and friends, how would you describe the majority opinion on COVID-19 vaccination? [*Social conformism*]	1	Very skeptical	
		2	Rather skeptical	
		3	Skeptical and favorable opinions are represented equally	
		4	Rather favorable	
		5	Very favorable	
C5	If the government encourages me to get vaccinated, it… [*Confidence in system*]	1	Encourages you to do it	1 = Completely dissuades you; 5 = Completely encourages you
		2	Has no effect on you	
		3	Dissuades you	

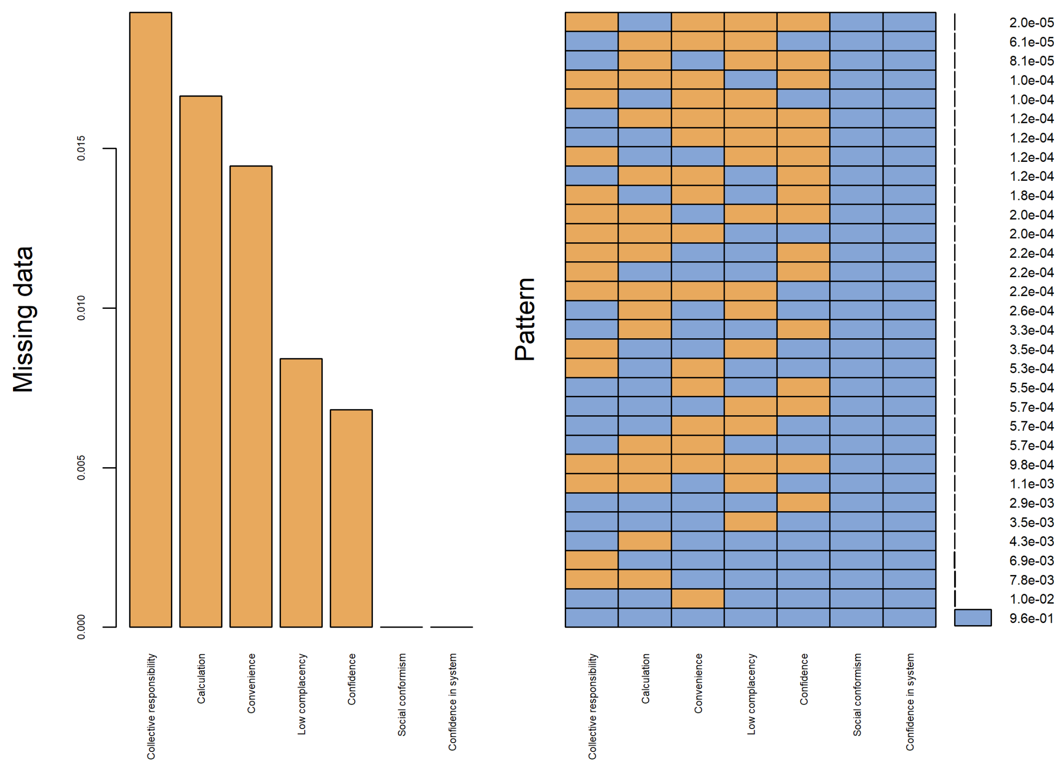
Colour Legend	General characteristics variables	Outcome variables	7C variables

Appendix 2. Missing data graphical representation obtained from: (a) Missing data of sociodemographic and health-related variables, (b) Missing data of the 7C antecedents. Both graphs show the proportion of missing values by variable (left side) and the pattern of missingness (right side). Orange represents that data is missing for that variable in the pattern and blue that data is present; the row side bar indicates the proportion of each missingness pattern. This pattern allows visualise if data is missing or not at random. Graphs (a) shows that missingness is concentrated in few variables, while in graph (b) missing data is more spread. Note: The variable uptake speed, included in graph (a) is not part of the analysis performed in this thesis.

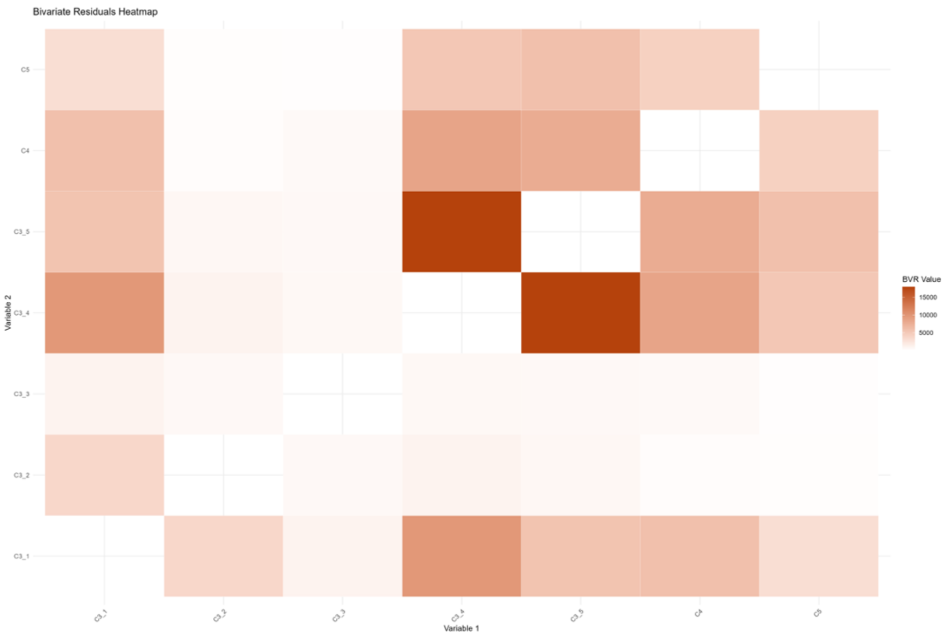
(a)



(b)



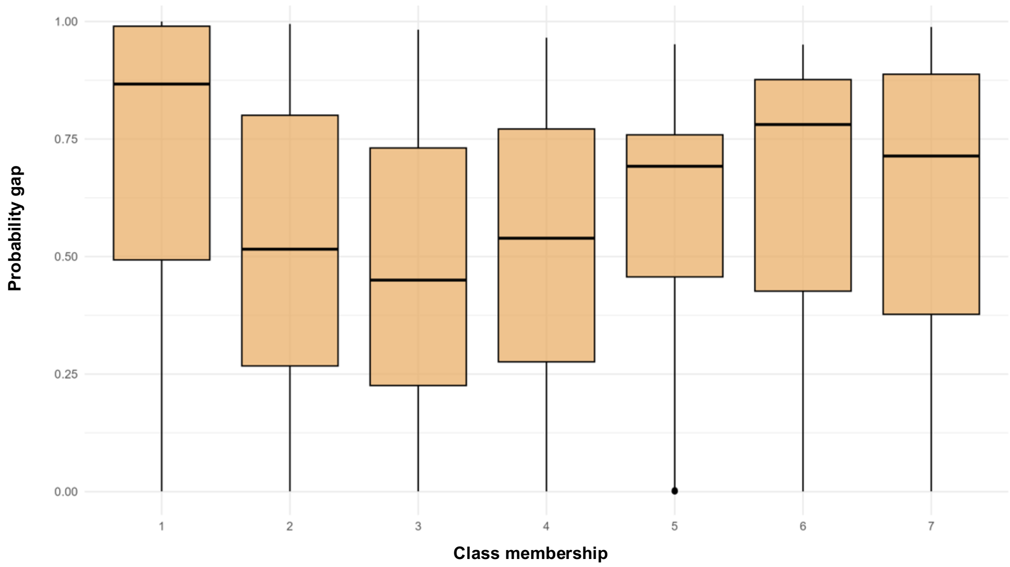
Appendix 3.



The graph presents the bivariate residuals (BVRs), which assess whether associations between variables persist after accounting for the latent classes. All BVR values exceed the threshold of 3.84, indicating potential violations of the local independence assumption and suggesting the presence of unexplained structure within the model. Nonetheless, the model retains epidemiological relevance and considers the statistical guidelines for model fit, thereby supporting the validity and practical utility of the identified attitudinal profiles.

Appendix 4. Graphs and tables showing the probability gap by (a) class membership, and (b) according to an established (0.1) threshold for data segmentation.

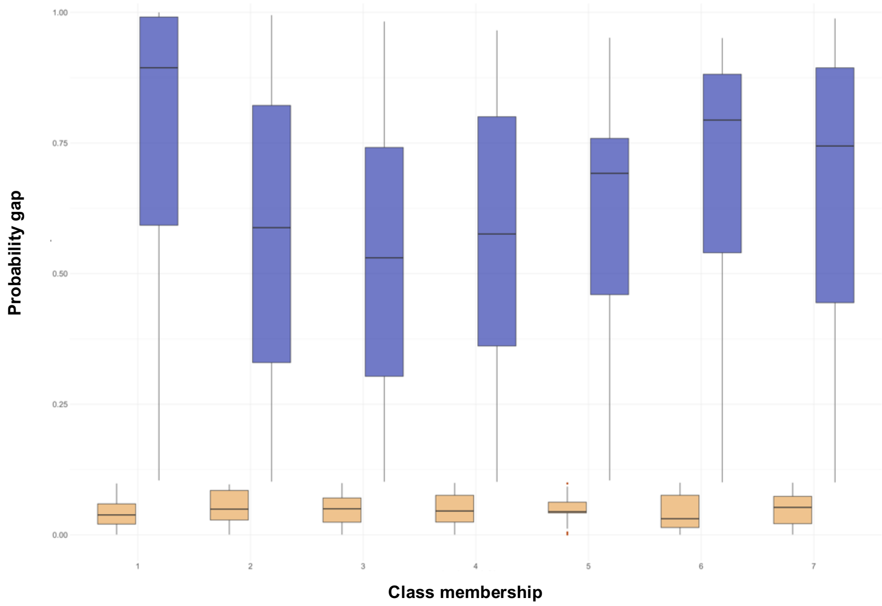
(a) Probability gap by class membership



Probability gap by class membership				
Class	**Count**	**Mean Probability gap**	**Median Probability gap**	**SD Probability gap**
1	1149	0.72	0.87	0.32
2	2248	0.53	0.52	0.30
3	2149	0.48	0.45	0.29
4	5359	0.52	0.54	0.28
5	9145	0.62	0.69	0.24
6	9098	0.65	0.78	0.29
7	3560	0.63	0.71	0.29
Total	32708			

According to the boxplot and the values observed in the table, the mean probability gap is higher for class 1 (0.72) and lower for class 3 (0.48), suggesting higher and lower confidence in probability assigment, respectively. Although median values are close to mean values, they are highlight skewed. Especially, the median in class 1, which is higher (0.87), suggesting that a large portion of this group has higher probability gaps. The Standard Deviation (SD) values from the probability gaps range from 0.24 to 0.32, indicating the spread of probability gaps within each class. Class 1 also has the highest SD, meaning more variability in probability gaps. Therefore, classes 1, 5, 6, and 7 have higher average and median probability gaps, indicating that individuals in these groups have, on average, a more reliable probability assigment, while classes 2, 3, and 4 have lower mean and median probability gaps, suggesting more uniform assigment or less overall confidence.

(b) Probability gap by class using a 0.1 threshold to divide into ambiguous and confidence groups.

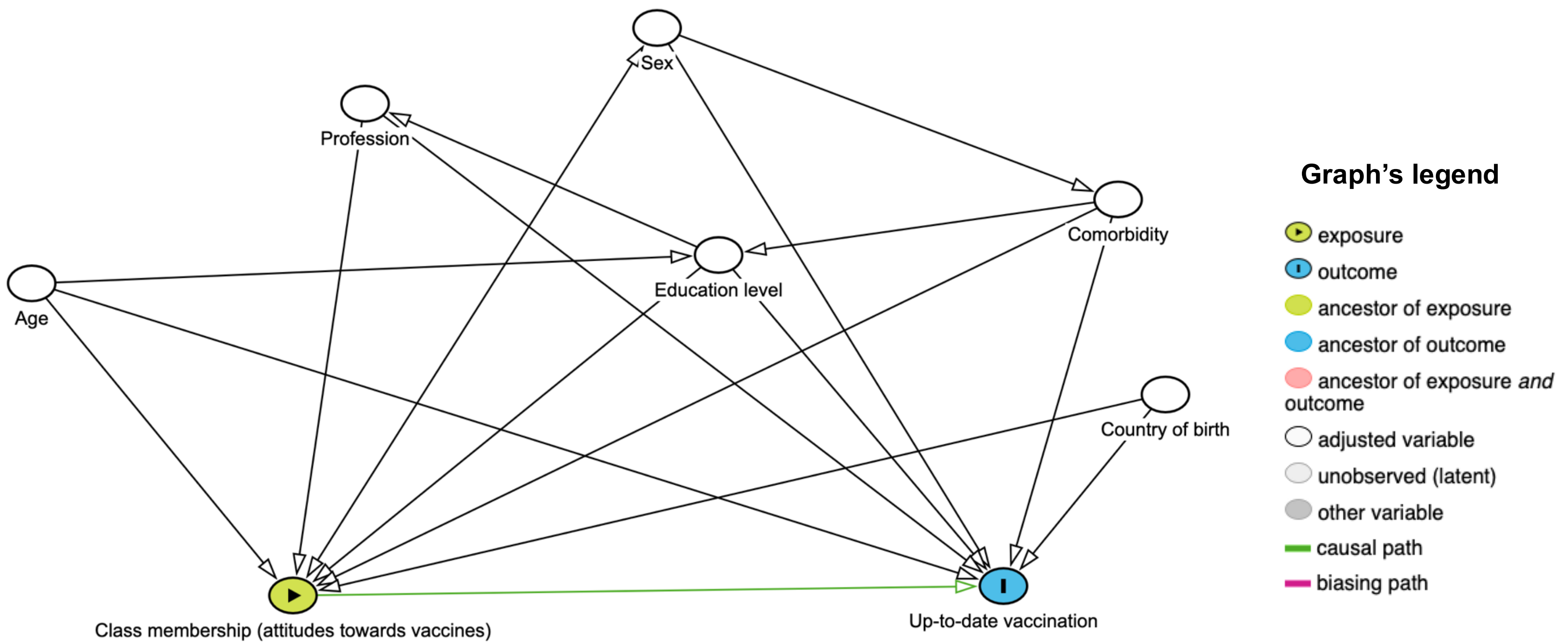


Summary of Ambiguous and Confident Groups by Class (Threshold 0.1):										
	Ambiguous					Confident				
Class	**Count**	**Prevalence (%)**	**Mean Gap**	**Median Gap**	**SD Gap**	**Count**	**Prevalence (%)**	**Mean Gap**	**Median Gap**	**SD Gap**
1	69	0.2	0.042	0.038	0.027	1080	3.3	0.767	0.894	0.273
2	194	0.6	0.053	0.049	0.030	2054	6.3	0.577	0.588	0.271
3	242	0.7	0.049	0.050	0.027	1907	5.8	0.531	0.530	0.262
4	435	1.3	0.050	0.046	0.028	4924	15.1	0.565	0.576	0.256
5	438	1.3	0.049	0.044	0.022	8707	26.6	0.646	0.692	0.208
6	562	1.7	0.041	0.031	0.029	8536	26.1	0.689	0.794	0.254
7	207	0.6	0.050	0.053	0.030	3353	10.3	0.662	0.744	0.265
Group Total	2147	6.6				30561	93.4			

By assigning a threshold to find those cases that were the most ambiguous, each class was divided into the ambiguous (low probability gap < 0.1) and confident group (high probability gap ≥ 0.1). As observed from the summary table, the former group involved a total of 2147 cases (6.6% of total) and the latter, 30561 cases (93.4% of total), showing that the prevalence of ambiguous cases is always much lower than confident cases. In addition, the boxplot shows the distribution of probability gaps for each class, in which we can observed that the confident group (blue) has wider and larger gaps, including higher medians, overall showing more variability and higher probability gaps. Meanwhile, the ambiguous group (orange) has more narrow, lower gaps and medians, and they are clustered near zero, which confirm the low probability gaps. Therefore, this boxplot and table clearly reflect a small ambiguous group with low gaps and a larger confident group with higher and more variable gaps.

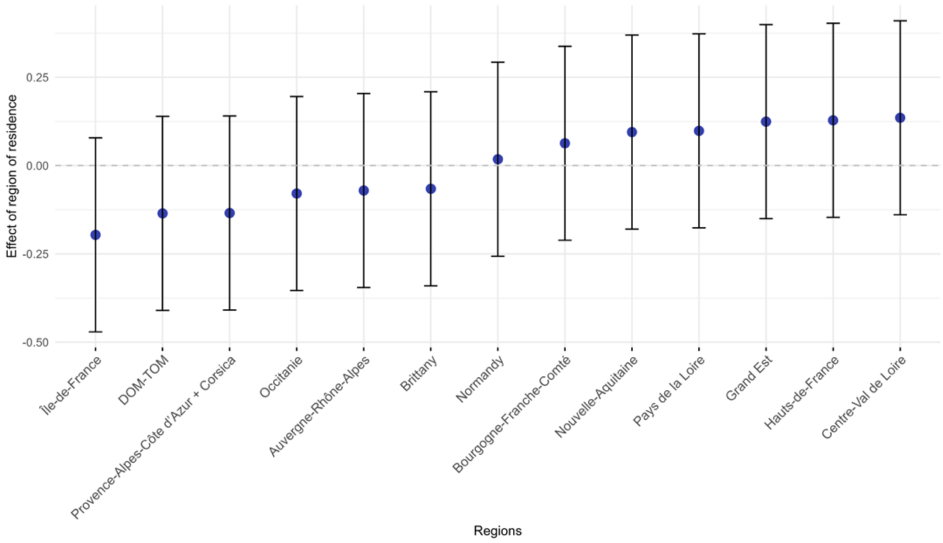
Appendix 5.

The rationale for the structure of this directed acyclic graph (DAG) is grounded in findings from Lamuda et al. (48), Lièvre et al. (9), and Roederer et al. (49), who reported that individuals who were early or timely vaccinators tended to be female, younger, more highly educated, less likely to have comorbidities, and were more often born in France. In addition, certain professional groups, particularly senior executives and intermediate professionals, were more likely to be vaccinated, while laborers had lower vaccination rates. As depicted in the DAG, these variables (age, sex, education level, profession, comorbidity, and country of birth) are modeled as potential confounders due to their associations both with class membership (attitudes towards vaccines) and with up-to-date vaccination status. The DAG illustrates that these sociodemographic and health-related factors may influence both the exposure (class membership) and the outcome (up to date vaccination status), either directly or indirectly. Therefore, we adjusted for these variables in the mixed-effects logistic regression model to account for their potential confounding effects and to provide an unbiased estimate of the association between class membership and up to date vaccination status.



Appendix 6.

The table and figure in this appendix show the effect of region of residence on being up to date with vaccination via conditional modes (random intercepts) with 95% CI indicating uncertainty in the estimates based on the variability of the data (conditional variance), but not providing inferential thresholds. This mixed effects model with regional random intercepts indicated slight deviations from the mean, with Île-de-France having the largest negative deviation (CM: -0.20; 95% CI: -0.47 – 0.08) and Centre-Val de Loire having the largest positive deviation (CM: +0.14; 95% CI: -0.14 – 0.41). Nevertheless, all the effects were very small, and all the CI ranges overlapped zero within ± 0.14, indicating only minor differences between regions after adjusting for the other model variables.



Region	Intercept	SE	CI lower	CI upper
Île-de-France	-0.20	0.14	-0.47	0.08
Centre-Val de Loire	0.14	0.14	-0.14	0.41
Bourgogne-Franche-Comté	0.06	0.14	-0.21	0.34
Normandy	0.02	0.14	-0.26	0.29
Hauts-de-France	0.13	0.14	-0.15	0.40
Grand Est	0.12	0.14	-0.15	0.40
Pays de la Loire	0.10	0.14	-0.18	0.37
Brittany	-0.07	0.14	-0.34	0.21
Nouvelle-Aquitaine	0.09	0.14	-0.18	0.37
Occitanie	-0.08	0.14	-0.35	0.20
Auvergne-Rhône-Alpes	-0.07	0.14	-0.35	0.20
Provence-Alpes-Côte d'Azur + Corsica	-0.13	0.14	-0.41	0.14
DOM-TOM	-0.14	0.14	-0.41	0.14

Appendix 7.

Condition number of the Hessian and Multicollinearity assessed through Generalized Variance Inflation Factor (GVIF) and adjusted GVIF ($GVIF^{(1/(2*Df))}$).

The **condition number of the Hessian** was slightly above the recommended caution threshold of 10^4 (**observed value: 11,022.5**). This does not indicate numerical instability, however, small effect estimates, and p-values should be interpreted with caution.

Collinearity was also assessed using the adjusted Generalized Variance Inflation Factor **($GVIF^{(1/(2*Df))}$)**, since all values were below 2.4 (see table below), which are under the commonly used threshold of 5, we can be confident that the results from this model are both interpretable and reliable.

Variable	GVIF	Df	GVIF^(1/(2*Df))
Class 1	4.01	1	2.0
Class 2	2.34	1	1.5
Class 3	2.23	1	1.5
Class 5	3.56	1	1.9
Class 6	2.63	1	1.6
Class 7	5.63	1	2.4
Sex	1.12	1	1.1
Age	3.11	5	1.1
Professions	4.40	7	1.1
Education	1.57	3	1.1
Country of birth	1.02	1	1.0
Comorbidities	1.08	2	1.0