



Area and individual level analyses of demographic and socio-economic disparities in COVID-19 vaccination uptake in Belgium

Pierre Hubin^{a,*}, Laura Van den Borre^{a,b}, Toon Braeye^a, Lisa Cavillot^{a,c}, Matthieu Billuart^a, Veerle Stouten^a, Léonore Nasiadka^a, Elias Vermeiren^a, Izaak Van Evercooren^a, Brecht Devleeschauwer^{a,d}, Lucy Catteau^a, Joris A.F. van Loenhout^a

^a Department of Epidemiology and Public Health, Sciensano, Brussels, Belgium

^b Interface Demography, Department of Sociology, Vrije Universiteit Brussel, Brussels, Belgium

^c Research Institute of Health and Society, University of Louvain, Brussels, Belgium

^d Department of Translational Physiology, Infectiology and Public Health, Ghent University, Merelbeke, Belgium

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ABSTRACT

Vaccination has played a major role in overcoming the COVID-19 pandemic. However, vaccination status can be influenced by demographic and socio-economic factors at individual and area level.

In the context of the LINK-VACC project, the Belgian vaccine register for the COVID-19 vaccination campaign was linked at individual level with other registers, notably the COVID-19 laboratory test results and demographic and socio-economic variables from the DEMOBEL database. The present article aims at investigating to which extent COVID-19 vaccination status is associated with area level and/or individual level demographic and socio-economic factors. From a sample of all individuals tested for SARS-CoV-2 (LINK-VACC sample) demographic and socio-economic indicators are derived and their impact on vaccination coverages at an aggregated geographical level (municipality) is quantified. The same indicators are calculated for the full Belgian population, allowing to assess the representativeness of the LINK-VACC sample with respect to the impact of demographic and socio-economic disparities on vaccination uptake.

In a second step, hierarchical models are fitted to the individual level LINK-VACC data to disentangle the individual and municipality effects allowing to evaluate the added value of the availability of individual level data in this context.

The most important effects observed at the individual level are reflected in the aggregated data at the municipality level. Multilevel analyses show that most of the demographic and socio-economic impacts on vaccination are captured at the individual level, although accounting for area level in individual level analyses improve the overall description.

Introduction

The development of safe and efficient vaccines against COVID-19 has played a major role in reducing the impact of the pandemic [1–7]. Large disparities have been observed in the uptake of COVID-19 vaccines both between countries, [8,9] but also within countries [9]. The within-countries disparities have among others been related to demographic, social, or economic differences [10–19]. Various approaches, based on aggregated data, [13,17] on individual data from surveys, [15,20] or on individual data from health registers, [10,12,14,18,19] generally lead towards the same conclusions that lower socio-economic statuses and

specific demographic situations (young age groups, people with a migration background) are associated with lower COVID-19 vaccine uptake. Despite these robust general patterns, there remains uncertainty about the importance and interplay of specific demographic and socio-economic factors. Studies building on aggregated indicators at various area levels [13,17] may be subject to ecological bias and therefore limited in their ability to pinpoint specific vulnerable social groups or identify how demographic and socio-economic characteristics interact. Individual level analyses allow more granular approaches but data are generally limited to a specific sample of the population within the framework of a specific study. For such situations, there is a question on

* Corresponding author at: Department of Epidemiology and Public Health, Sciensano, Rue Juliette Wytsman 14 1, 1050 Brussels, Belgium.

E-mail address: pierre.hubin@sciensano.be (P. Hubin).

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the representativeness of the study sample. Furthermore, a recent systematic review on vaccine hesitancy in the United States demonstrates the importance of factors at multiple socioecological levels [21]. A few studies have investigated individual and aggregated level characteristics simultaneously in the context of vaccination [22–25]. Social inequalities and regional disparities within the context of the COVID-19 pandemic in Belgium have also been observed with respect to several COVID-19 related health outcomes. More specifically, an investigation of COVID-19 incidence during the first three COVID-waves shows clear differences by area-level social deprivation [26]. Significant inequalities have also been observed in excess mortality during the first COVID-wave for persons with a low income [27,28] and from specific migrant groups [29]. To our knowledge, and at the time of writing, there has been no study on COVID-19 vaccination that disentangles individual and area characteristics of the demographic and socio-economic background. The current study addresses this knowledge gap with Belgium as case study. The primary schedule vaccination campaign against COVID-19 was considered successful in Belgium: on the 31st of October 2022, 86.4 % of the adult population had completed the primary schedule which ranked Belgium as the 7th country with the highest vaccination coverage in Europe [30]. Nevertheless, clear individual demographic (e.g. younger age groups, first generation migrants, lone adult or single parent households) and socio-economic disparities (e.g. lower education, lower income) were found in the uptake of COVID-19 vaccine [13,19]. Regional disparities in vaccine uptake have also been observed with Flanders (the northern part of the country) being generally associated with higher vaccination coverages compared to Brussels (center region), and to a lower extent Wallonia (southern region) [30].

In the context of the COVID-19 vaccination campaign, the LINK-VACC project was set-up by Sciensano, the Belgian institute for health, to perform the post-authorization surveillance of COVID-19 vaccines uptake and effectiveness in Belgium. To that aim, selected variables from multiple existing national health and social sector registers were linked at an individual level.

The main objective of this study, within the framework of LINK-VACC, is to investigate to what extent COVID-19 vaccination status is associated with area (municipality) and individual level demographic and socio-economic factors as well as their relative contributions. In parallel, we assess the representativeness of a sizable sample of the population based on COVID-19 testing register (LINK-VACC sample) in the context of analyzing the impact of social patterns on the COVID-19 vaccination campaign. The presented work offers new insights into the added value of the availability of individual level data to address such questions.

Material and methods

Data

Within the LINK-VACC project, selected variables from multiple existing national health and social sector registers are linked at an individual level based on the unique Belgian social security number within a pseudonymized environment hosted by healthdata.be, a data platform within Sciensano [31]. The present study relies on variables originating from three databases: 1) The Belgian vaccine register (Vaccinnet +), containing data on COVID-19 vaccine doses administered to Belgian residents as well as demographical data on the vaccinated person, 2) the COVID-19 healthdata.be test database, containing data from COVID-19 laboratory test performed in Belgium as well as demographical data on the tested person, 3) the DEMOBEL database provided by Statistics Belgium (Statbel) containing variables related to demographic and socio-economic indicators as well as information on the national register status for Belgian residents vaccinated or tested at least once at time of linkage. Detailed definitions of variables available in the framework of this study have been described in a previous work [19]. Complementary to 3), a dataset aggregated at the municipality, i.e. Local Administrative

Units-2 (LAU-2) geographical level, containing counts of individuals by each level of the relevant demographic and socio-economic variables based on exhaustive data for the registered Belgian population, and for the same time period, was also made available from the DEMOBEL database. The number of persons vaccinated at the municipality level for the full population was available from Sciensano open data resources. A scheme representing the data sources and datasets used in this study is provided in [supplementary material \(Scheme S1\)](#).

Study population

The study population for the individual level analyses consists of all individuals residing in Belgium aged 18 years and over, tested at least once for SARS-CoV-2 (by PCR or antigen test) in Belgium before the 31st of August 2021, and for whom successful linkage with the DEMOBEL database was made. Individuals deregistered, migrated, or deceased before this date based on their status in the national register, or those with unknown municipality of residence were excluded. Finally, during exploratory analysis, one municipality was identified as outlier due to its very small population (less than 100 persons). To be consistent, all individuals from this municipality were also excluded from the analyses, resulting in a final sample of 5,313,607 persons. It is important to note that individuals that were not tested or vaccinated are not captured in the LINK-VACC database. To minimize the overestimation of vaccination rates, individuals who were vaccinated, but not tested are excluded from the study population.

Outcome

The outcome for this cross-sectional study is based on the vaccination status (having received one dose or not) on 31st August 2021 according to the Vaccinnet + register. On 31st August 2021, all individuals of 18 years and over officially residing in Belgium had received an invitation to be vaccinated with a first dose and the opportunity to receive it. Therefore, individuals who had not received a first dose of vaccine by that date are considered as not vaccinated. Administration of a first dose is a good predictor of a full primary course of vaccination since nearly all individuals who received at least one dose completed their primary schedule [19]. The response variable modeled in the logistic models presented here corresponds to the proportion of people not vaccinated.

Statistical analyses

From the LINK-VACC sample, data are aggregated at the municipality level including counts of individuals by vaccination status and by each of the demographic and socio-economic categories (*agg sample*). A similar dataset at the municipality level is available for the full Belgian population (*agg pop*). Tables defining all naming conventions and abbreviations and a description of the variables throughout the study are provided in [supplementary material \(Tables S1 and S2\)](#).

To assess the representativeness of the sample originating from tested individuals, pairwise Spearman's rank correlation coefficients are computed between vaccination rates and every socio-economic and demographic indicators selected at the municipality level within both *agg sample* and *agg pop* datasets. In a second step, logistic regression models are fitted to both *agg sample* and *agg pop* datasets. To this end, each municipality is attributed a score computed as the sum of the standardized proportions (i.e. z-scores) of people with migration background, households with low income, and households with only one adult in the municipality; three descriptors correlated with each other and individually associated with lower vaccination rates. A categorical variable is then derived from the score by grouping municipalities into quartiles of it. The models (A and B) include this categorical descriptor as explanatory variable together with region (a three-level categorical variable), age (standardized median age in the municipality), and sex

(standardized proportion of male individuals).

To investigate the relative importance of individual and area level, logistic regressions models are fitted to the individual level data: a model including only fixed effects (C), a model with only one random municipality effect (D), a hierarchical model with both individual level fixed effects and the random municipality term (E), and finally another hierarchical model including also the indicators derived at the municipality level as additional fixed effects (F). A listing of the different models fitted to aggregated and individual level data is provided in Table 1.

Wald 95 % confidence intervals (CI) are reported. Robustness of the standard error estimates is assessed by calculating heteroscedasticity-consistent estimates and/or running bootstrap analyses. All numerical values of the ORs and corresponding CI from the models are provided in supplementary material (Table S3). All analyses were performed in R (version 4.0). Hierarchical models were fitted with the lme4 package [32]. Corrections for heteroscedasticity-consistent standard errors were computed using the Sandwich package, [33] R^2 statistics of the different models with the r.squaredGLMM function of the MuMin package [34].

Results

In the following section, we first detail the results obtained based on the datasets aggregated at the municipality level *agg_sample* and *agg_pop*. In a second step, the results of the multilevel analysis are detailed.

Aggregated level analyses

As a descriptive analysis, Fig. 1 shows maps illustrating the full Belgian population data for vaccination status and the three proportions included in the definition of the score defined in method section: each of the 581 Belgian municipalities are colored by proportion of 1) not vaccinated individuals (*p_notVacc*), 2) people with a migration background (*p_migrationBG*), 3) people with a low income (*p_incomeLow*), and 4) one person and single parent households (*p_hhLone*). Some patterns are consistently found on all maps indicating positive correlations between the migration background, low income, and lone adult household indicators; as well as a positive correlation between these indicators and the proportion of individuals not vaccinated. Contrast is also seen between regions on the maps, and is stronger for the proportion of vaccinated people compared to the other indicators. The pairwise Spearman’s rank correlations between variables of each dataset is shown in Fig. 2. It also shows the pairwise correlations of the same variable between each dataset on the diagonal. These pairwise correlations are consistent for the proportions derived from both datasets. Focusing specifically on the correlations of proportion of not vaccinated with the proportions related to demographic and socio-economic indicators, low income ($\rho = 0.717$), migration background ($\rho = 0.700$), and lone adult households ($\rho = 0.696$) are the three indicators with the largest correlations in *agg_sample*, and are comparable in

agg_pop dataset (0.666, 0.716, and 0.736). The median age is negatively correlated with the proportion of not vaccinated with coefficients of -0.394 and -0.555 in *agg_sample* and *agg_pop*, respectively. A table summarizing the percentages of individuals in the not vaccinated, with migration background, low income, lone adult household, percentages of male individuals, and median age in Belgium for both datasets is also provided in supplementary material (Table S4). Small discrepancies are observed, notably for the overall percentage of people not vaccinated or the median age (both larger in *agg_pop*).

The results of the multivariable analyses performed on the aggregated datasets (models A and B) are shown in Fig. 3. ORs greater than 1 indicate a higher probability of the population in the group of not being vaccinated. Both datasets show consistent trends in view of the score quartiles. A municipality belonging to a higher quartile is expected to have larger proportions of residents with a migration background and/or with a lower income and/or living alone or being a single parent which is strongly associated with a lower probability of being vaccinated for the inhabitants of that municipality. The regional aspect is also important, the largest OR computed being the one associated with the municipalities in the Brussels region (with Flanders region as the reference). A higher proportion of men relates to a slightly lower probability of being vaccinated. Overall, there is no major discrepancy between the results obtained from the model fitted to *agg_sample* or *agg_pop*, although larger estimates are observed from the full population data consistent with the overall higher proportion of individuals not vaccinated in the full population.

Multilevel analyses

Fig. 4 shows the ORs and their corresponding 95 % CI for models A and C-F. Model A is fitted to the *agg_pop* dataset and corresponds to light green colored estimates in Fig. 3 (full Belgian population). Model C was the subject of an earlier work and is extensively discussed there [19]. Most of the demographic and socio-economic descriptors investigated within this model impacts the tendency of being vaccinated. Notably, the fact of having a migration background (of first and to a lesser extent second generation) or having a low income increase the probability of not being vaccinated. These trends are reflected in the ORs of the score quartiles variable in the models that were fitted to aggregated data. A gradient in age is also observed, the probability of being vaccinated being the highest in the 75–84 age group and the lowest in the 25–34 age group. Model D only includes a random municipality effect. Model E adds the municipality random component to the fixed effects of model C. Finally, model F adds the descriptors from municipality level to model E. The random effect variances, Median Odds Ratio (MOR), [35] R^2 statistics, and Bayesian Information Criterion (BIC) of models C-F are collated in Table 2. The proportion of variance explained by the fixed effects (R^2 fixed) decreases upon addition of the random effect in the model (C versus E), and increases when municipality-level indicators are included in the model (F). Consistently, the random effect variance is

Table 1
Summary of logistic regression models, by type of effects, level of aggregation, and source of data.

		Model A	Model B	Model C	Model D	Model E	Model F
Outcome	Vaccination	M	M	I	I	I	I
Indicators	Migration background	M	M	I		I	I & M
	Missing income			I		I	I
	Income	M	M	I		I	I & M
	Household composition	M	M	I		I	I & M
	Sex	M	M	I		I	I & M
	Age	M	M	I		I	I & M
	Region	M	M	I		I	I
	Total population	M	M				
	Data sources	Full population	LINK-VACC	LINK-VACC	LINK-VACC	LINK-VACC	LINK-VACC + Full population
Effects	Fixed	Fixed	Fixed	Random	Fixed & random	Fixed & random	
Descriptors	cont & cat	cont & cat	cat	cat	cat	cont & cat	

Abbreviations: Municipal level variable (M); Individual level variable (I); Continuous descriptor (cont); Categorical descriptor (cat).

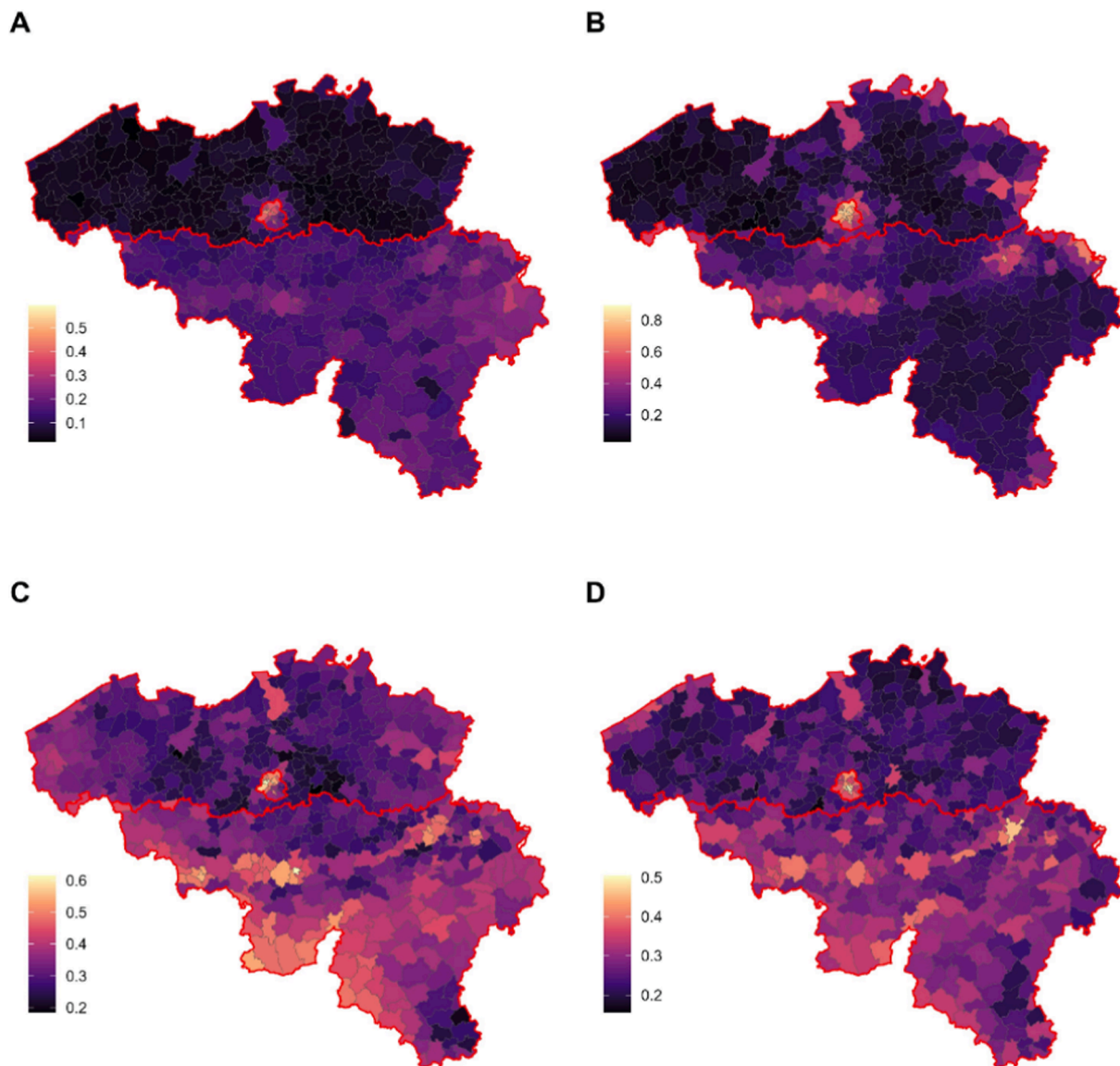


Fig. 1. Maps showing proportions at the municipality level of individuals not vaccinated (A), of individuals with a migration background (B), of individuals with a low income (C), and of lone adult households (D) from the full Belgian population. Regional borders are indicated with red lines: Flanders is situated in the North, Wallonia in the South, and Brussels in the center. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

larger when only individual level fixed effects are included in the model (E versus F). In Fig. 4, it is seen that the overall average region fixed effect (*regWal* and *regBru*) decreases when the random municipality effect is included in the model as part of the variability associated with the place of residence is captured by the municipality term. The estimates related to migration background or low income are also impacted by including the municipality level explicitly in the model (models E and F), but to a lower extent compared to the region fixed effect.

The estimates of the fixed effect descriptors characterizing the municipality level are comparable in the model fitted to aggregated or individual level data, except for the fourth quartile of the score variable which does not significantly differ from the third quartile in model F while a clear difference is seen in the model fitted to aggregated data only (model A).

95 % Wald CI intervals are presented in this section, including an heteroscedasticity-consistent corrections for CI originating from the aggregated level analyses. Further discussions on reliability of the standard error calculations is provided in [supplementary material \(Figure S1\)](#).

Discussion

This study sheds light into the relevance of relying on individual and area levels demographic and socio-economic factors to explain COVID-19 vaccination patterns. It also provides an assessment of the representativeness of a sample based on the population tested at least once for SARS-CoV-2 (LINK-VACC).

The multilevel analyses revealed that both individual and municipal characteristics of the demographic and the socio-economic background are relevant factors in COVID-19 vaccination research. Overall, similar conclusions are drawn from both levels, however individual-level data allow for a more granular approach as well as more statistical power. The individual demographic and socio-economic situation appears to be the main driver for vaccine uptake from our results, especially migration background, income, and age. Adding municipality characteristics as additional fixed effects in the hierarchical model already containing individual level descriptors does not affect the fit to the data much. Nevertheless, it is seen from the results of model F that individuals living in municipalities belonging to the higher quartiles of the summarized

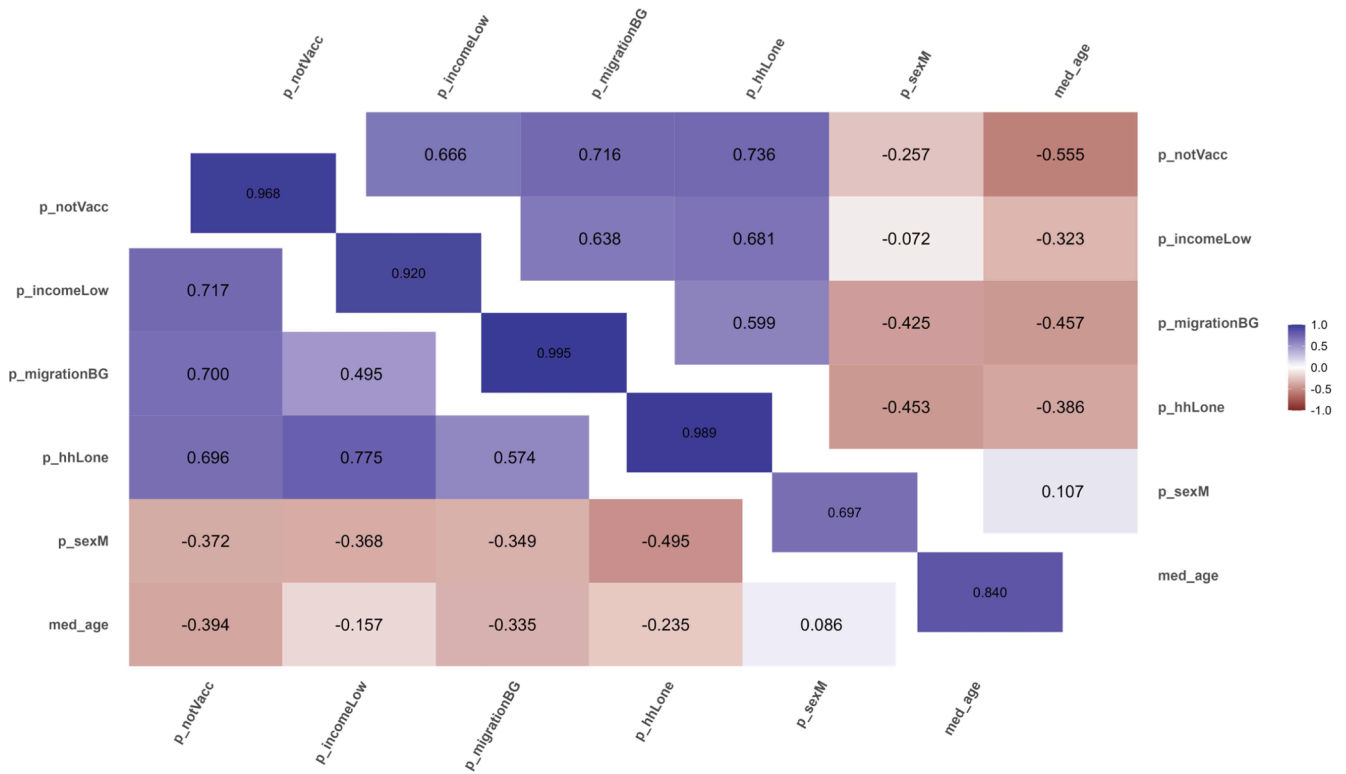


Fig. 2. Spearman's rank correlation coefficients (rho) of proportion of not vaccinated and several descriptors from *agg_sample* (lower triangle) and *agg_pop* (upper triangle) datasets. The diagonal elements shows the correlation between the same variables of each dataset.

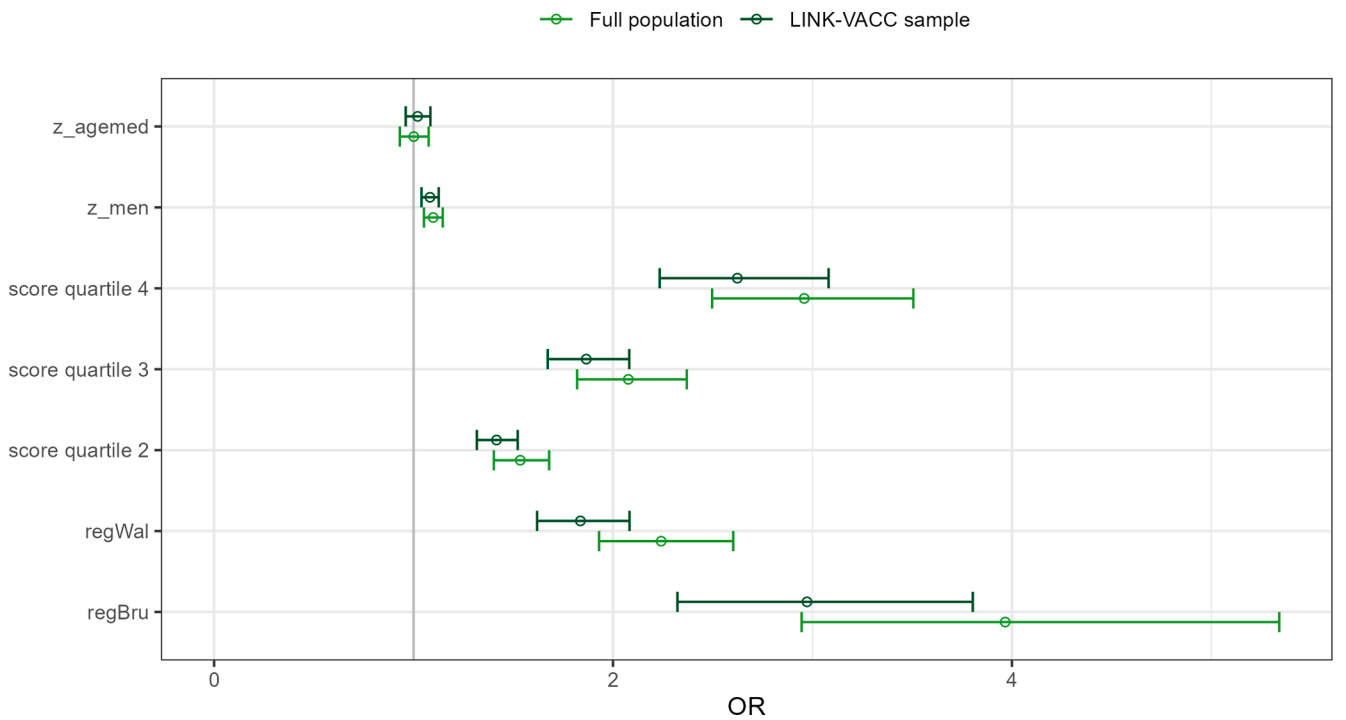


Fig. 3. ORs and 95% CI of models fitted to the aggregated datasets, corresponding to models A and B for Full population and LINK-VACC sample, respectively. CI are computed from heteroscedastic robust standard errors.

score (derived from migration background, income, and household composition) are more likely of not being vaccinated. More generally, the importance of the random municipality term in models E and F shows that it explains part of the variability in the vaccination outcome

that is not captured by the other terms. Such initial results indicate a potential neighborhood effect in the context of COVID-19 vaccination which may be investigated further [36].

With regard to the sample based on the tested population (LINK-

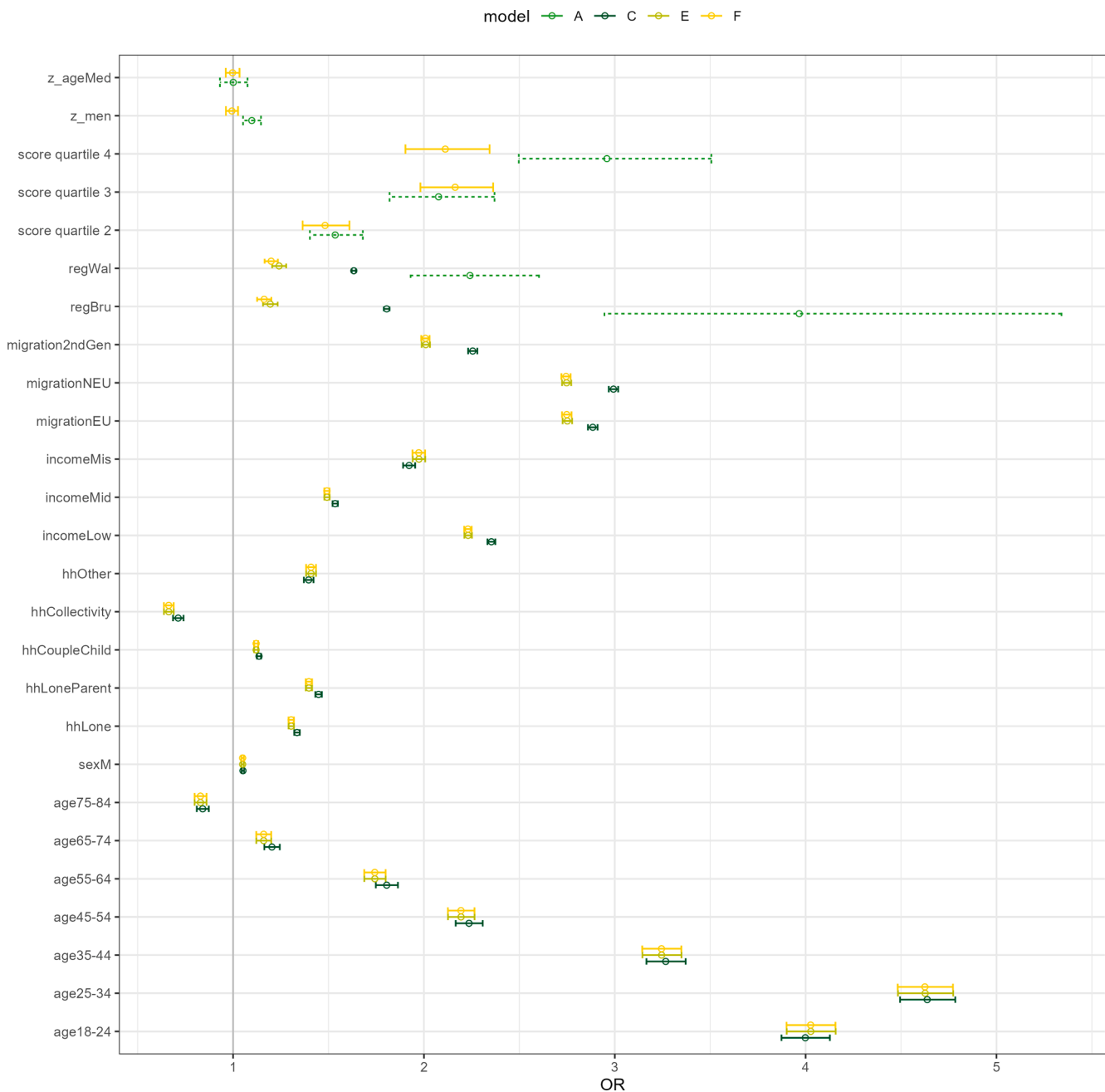


Fig. 4. ORs and 95% CI of models fitted to individual and municipality level data. Dashed lines corresponds to ORs from model A fitted to aggregated data only.

Table 2
Random effect variances, Median Odds Ratio (MOR), [35] R² statistics, and Bayesian Information Criterion (BIC) of the 4 models fitted to individual level data.

Model	Random effect variance	MOR	R ² fixed	R ² tot	BIC
C	0	1	0.2264	0.2264	1133461
D	0.4007	1.8291	0	0.1086	1364313
E	0.2109	1.5497	0.1938	0.2424	1085249
F	0.1175	1.3868	0.2278	0.2545	1084594

VACC data), our analyses show that it provides a reliable representation of the impact of the demographic and socio-economic indicators on COVID-19 vaccination. The analyses of aggregated data, the consistency of correlations coefficients, and logistic regression models provide robust results for this representativeness.

The strong region effect observed in the raw numbers and confirmed in this study is worth to be discussed further. Higher coverages have generally been achieved in all age groups in Flanders compared to Wallonia and especially Brussels consistently throughout the COVID-19 vaccination campaigns. Given that demographic and socio-economic disparities exist between regions, the hypothesis can easily be made that they explain most of the difference in vaccination coverages observed between regions. Our results indeed show that the regional effect becomes less important when individual level social disparities are taken into account. However, a significant region effect appears in all models suggesting that regional disparities in vaccination rates are not completely explained by the demographic, socio-economic, and municipality effects included in this study. Organizational aspect of the vaccination campaign and/or cultural background, such as language differences, not captured in the data may also play a role.

The LINK-VACC database which included a total of 10,475,908

individuals at the time of data linkage is one of the main strength of this study. It allowed to run the analyses on a sizeable sample of 5,313,607 individuals after applying the inclusion criteria described in the Materials and method section. As comparison the total Belgian population was officially 11,521,238 on 1st January 2021, and the reference adult population included in this study 9,209,116. The possibility to perform a data linkage based on the national security number is another strength ensuring the quality of the linking process [19]. In terms of method, the combination of aggregated and individual data in the same study is another asset, as there are few examples of studies applying such method in the literature related to impact of social disparities on vaccination.

The main limitation in terms of data availability resides in the fact that individuals who were never vaccinated or tested are not in the LINK-VACC database. As a consequence vaccination rates calculated at the municipality level are by default larger within LINK-VACC since a share of the individuals not vaccinated cannot belong to the sample. Nevertheless, as stated above, the analyses at the aggregated level show a good representativeness of the full Belgian population. It should also be pointed out that registration in the national vaccine COVID-19 register is possible but not mandatory for persons vaccinated abroad (e.g. frontier worker). This could result in a slight underestimation of vaccination coverages in specific groups.

Various approaches can be considered to aggregate data from the individual to the municipality level, approaches similar to the one considered here, i.e. deriving a composite score from several indicators, have been used elsewhere [37,38]. More specifically, deprivation scores in the context of health inequalities have recently been defined for Belgium but at smaller area level than the municipality considered in this study (i.e. the statistical sector) [36]. Further research on this dataset may be useful to systematically assess which summarizing approach allows the best possible representation of the individual level data. Indeed, relying on summary statistics at an area level implies underlying assumptions on the distribution of the related covariates at the individual level. Therefore what is inferred from the aggregated level analyses may depend on the summary statistics used. The present work also underlines that such assumptions do not need to be made when individual level data are available.

The analyses presented here are limited to one point in time and one vaccination campaign. Further research could focus on adding a time component in the analysis taking into account the time to vaccination as well as multiple vaccination campaigns including boosters.

Conclusions

Comparison of results obtained from aggregated data at the municipality (LAU-2) level, individual level, and the combination of both shows that main conclusions drawn from aggregated level analyses reflect what can be found from the individual level data. Nevertheless, relying on the individual level enables more detailed categorizations of the variables. Accounting for area level in individual level analyses allows a more accurate estimation of the effects. Analyses performed on the aggregated data level show the representativeness of a sample based on individuals tested for SARS-CoV-2 for the full Belgian adult population on demographic and socio-economic indicators and their impact on vaccination. Regional differences in the COVID-19 vaccination campaign in Belgium are partly explained but not completely captured by the demographic and socio-economic indicators available in this study.

CRedit authorship contribution statement

Pierre Hubin: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Laura Van den Borre:** Writing – review & editing, Methodology, Conceptualization. **Toon Braeye:** Writing – review & editing, Methodology. **Lisa Cavillot:** Writing – review &

editing, Data curation, Conceptualization. **Matthieu Billuart:** Writing – review & editing. **Veerle Stouten:** Writing – review & editing. **Léonore Nasiadka:** Writing – review & editing. **Elias Vermeiren:** Writing – review & editing. **Izaak Van Evercooren:** Writing – review & editing. **Brecht Devleesschauwer:** Writing – review & editing. **Lucy Catteau:** Writing – review & editing. **Joris A.F. van Loenhout:** Conceptualization, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Individual level data are not publicly available and access requires a specific authorization by the Belgian Information Security Committee (ISC). The codes and aggregated datasets used in these analyses can be provided upon request.

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Ethics approval.

The protocol of the LINK-VACC project was approved by the Medical Ethics Committee from the Vrije Universiteit of Brussels on 3 February 2021 (B.U.N 1432020000371) and obtained authorization from the Information Security Committee (ISC) Social Security and Health (reference number: IVC/KSZG/22/166). The study protocol has been preregistered on ClinicalTrials.gov (ClinicalTrials.gov ID: NCT05373420).

As confirmed by sections 23 and 24 of the Guidelines 03/2020 on the processing of data concerning health for the purpose of scientific research in the context of the COVID-19 outbreak of the European Data Protection Board (V1.0 of 21 April 2020), this survey falls under Article 6 §1(e) and Article 9 §2(i) of the General Data Protection Regulation (GDPR). In appliance with these GDPR legal grounds of data processing, no informed consent had to be signed by the patients.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jvaxc.2024.100496>.

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