Access to healthcare as an important moderating variable for understanding geography of immunity levels for COVID-19 - preliminary insights from Poland

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Abstract

Background. Underascertainment of COVID-19 burden and uncertainty in estimation of immunity levels is a known and common phenomenon in infectious diseases. We tested to what extent healthcare access (HCA) related supply/demand interfered with registered data on COVID-19 from Poland.

Material and methods. We have run a multiple linear regressions model with interactions to explain geographical variability in seroprevalence, hospitalization (on voivodeship –NUTS-2– level) and current (beginning of the 4th wave –15.09-21.11.2021) case notifications/crude mortality (on poviats –old NUTS-4– level) taking vaccination coverage and cumulative case notifications till so called 3rd wave as predictor variables and supply/demand (HCA) as moderating variables.

Results. HCA with interacting terms (mainly demand) explained to the great extent the variance of current incidence and most variance in case of current mortality. HCA (mainly supply) is significantly moderating cumulative case notifications till the 3rd wave explaining the variance across seroprevalence.

Conclusions. Seeking causal relations between vaccination or infection gained immunity level and current infection dynamics could be misleading without understanding socioepidemiological context such as the moderating role of HCA (sensu lato). After quantification, HCA could be incorporated into epidemiological models for better prediction of real disease burden.

Keywords: healthcare access, health inequalities, COVID-19, statistical modelling, immunity level, quasi-causal diagrams

Background.

Knowing immunity levels is important for proper prediction of the COVID-19 dynamics for a given region. Researchers proposed multiple methods and models combining natural immunity possibly acquired after infection with induced immunity by various vaccines taking into account their interactions as well as various immunity waning schema [1,2]. We do know quite well how various vaccines are waning efficacy [3] against symptomatic infections (controlled for covariates such as seasonality or virus variants), however post-infection immunity is much more difficult to assess [4]. Seroprevalence studies can be also used to estimate immunity levels, previously having been heavily used attempting to estimate IFR (Infection fatality rate [5,6]).

From epidemiological practice, we already know that registered disease case notifications are not covering the real burden of infections to the same extent in various geographical locations due to socio-economic-medical inequalities [7]. Thus, healthcare access (HCA) has been already identified as a possible factor influencing measurable COVID-19 epidemic indexes and explaining intra-country variation [8–11]. For example, more resource-rich regions were able to organize both testing and treating capacities [12] and vaccination campaigns [13] in a faster and more inclusive way, whereas resource-poor regions were much more selective in the pandemic healthcare services delivery.

Surprisingly, HCA was not taken into consideration in infection dynamics modelling practice to much extent yet [11]. While immunity is gained and lost at the individual level, immunity level often is tried to be quantified at a population level, for instance, by accounting for biased measures such as estimates of undiagnosed cases or eliciting seroprevalence surveys. Wrong estimates of COVID-19 immunity levels varying over time and regions makes predictions challenging and significantly reduces predictive power. Thus, forecasts results are often far from reality, as was the case in Poland between June–September 2021 [14]. Moreover, recently some ecological studies are suggesting a weak or no link between vaccination coverage and current epidemic dynamics in the general populations, which has gained a lot of controversy and our observations puts a new light on it [15].

Material and methods.

We show on the example of Poland that **omitting HCA confounding factors could lead to misinterpretation in understanding current epidemic dynamics due to biased estimation of immunity levels**.

Data obtained from Polish registries on 16 voivodeships (NUTS-2) and 380 poviats (old NUTS-4):

- **Cumulative No. cases per capita**: The cumulative numbers of COVID-19 notifications till the so-called 3rd wave of epidemic (04.03.2020 15.06.2021) for poviat or voivodeship [16] divided by its population size.
- Healthcare Access Supply (supply HCA): The number of physicians working in health care per 10,000 inhabitants as an indicator of the supply HCA for poviat or voivodeship [17]. This is a good proxy for capacity and accessibility of healthcare services (public and private).
- Healthcare Access Demand (demand HCA): The number of consultations in primary care provided in 2019 for poviat or voivodeship divided by its population size

as an indicator of demand HCA [17]. Pearson correlation on demand HCA in 2019 and 2020 is 0.998 [13], so no significant regional changes have been observed in the demand for HCA due to the pandemic. Demand HCA is a complicated conglomerate of attitudes towards healthcare (i.e. level of trust in the effectiveness of offered treatment by public healthcare), perception of accessibility (i.e. how easily one can reach healthcare facilities), burden of disease (i.e. elderly and inferior health populations seek healthcare more often) and others (i.e. constrains and limits provided by National Health Fund).

- **Fraction of vaccinated:** Percentage of vaccinated with at least one dose for poviat or voivodeship (at the end of 3rd wave as of 15.06.2021) for all age groups [18]. Vaccination coverage gives us a proxy of proportions of population which gain post-vaccination immunity before the so-called 4th wave.
- Normalized incidence Sep/Oct'21: 2-week incidence of COVID-19 notifications (21.09–04.10.2021) during the beginning of the so-called 4th epidemic wave for a poviat [16].
- Normalized deaths Sep/Nov'21: Crude mortality rate Cumulative number of COVID-19 death cases (15.09–21.11.2021) during the so-called 4th epidemic wave per poviat divided by its population size [19].
- **Normalized Hospitalizations**: Number of occupied hospital beds (14.10.2021) at the beginning of the so-called 4th epidemic wave per voivodeship divided by its population size [20].
- Seroprevalence Obser-Co: The fraction of seroconverted [21] per voivodeship in a random (by design) sample as a proxy for immunity level collected during 29.03–14.05.2021. As this was the end of the 3rd epidemic wave, as well as the vaccination roll-out was at the beginning, this variable is a good proxy of post-infection acquired immunity.

The dynamics of SARS-CoV-2 spreading vary across the spatial clusters [12] and initial conditions as number of index cases and immunity levels could lead to different phases at the beginning of each wave. Thus, supply/demand HCA are assumed to be moderating variables that affect the relationship between independent (vaccine or post-infection immunity at the end of 3rd wave) and dependent variables (seroprevalence and the 4th wave outbreak dynamics indexes).

Results.

In a series of diagrams, we depict the explained share of variance for selected dependent variables of interest as calculated by multiple regression. The following predictor variables were used: vaccination coverage, cumulative case notifications, moderating terms supply/demand HCA as well as 2- and 3-way interactions among them (Fig. 1-4).



Figure. 1) Explained variance of seroprevalence at the end of 3rd wave – immunity level estimation from Obser-Co [21] on voivodeship level.

HCA (mainly supply) is significantly influencing seroprevalence survey results (Fig. 1), and 11% of variance is explained by the interaction between cumulative cases notifications and supply HCA. Most of the variance in seroprevalence is explained by cumulative cases notifications (vaccination was in a very early stage at the time of seroprevalence survey).



Figure. 2) Explained variance of hospitalizations during the 4th wave on voivodeship level.

Hospitalizations seem to be well predicted by vaccination coverage and cumulative cases notifications (52% of variance considering also the interaction between them). HCA (mainly supply) is influencing hospitalization (Fig. 2), but 15% of variance is explained by interaction between vaccination coverage and supply HCA.



Figure. 3) Explained variance of normalized case notifications (14-days incidence) during the 4th wave on poviat level.

HCA (mainly demand) is extremely important (Fig. 3, 4) to predict current infections dynamic (incidence and mortality). This is worth to stress that direct links between vaccination coverage as well as cumulative case notifications with current incidence are statistically negligible (only interactions with these terms have some impact).



Figure. 4) Explained variance of crude mortality rate during the 4th wave on poviat level.

Crude mortality rate (Fig. 4) in comparison to incidence (Fig. 3) during the beginning of the 4-th wave is less prone to the confounding effect of HCA. We can see a significant link (Fig. 4) between vaccination coverage and crude mortality rate due to COVID-19.

Conclusions.

There are multiple possible mechanisms explaining mediating role of HCA (however causal statements cannot be defined as probably both explaining and explanatory variable seems to depend on HCA):

- In regions with high availability of healthcare workers (supply HCA) patients are more likely to be sampled as seroconverted (Fig. 1), have higher chance to find a hospital bed (Fig. 2), as well as chance of being tested (and get positive result) increases a little (Fig. 3).
- Case notifications as well as in some extent crude mortality (Fig. 3, 4) are highly correlated with the way how patients are likely to use the public healthcare system

(demand HCA), thus in regions with low demand HCA real number of infections seems to be underestimated by documented case notifications to a higher extent than in places with high demand HCA.

Concluding each epidemiological index is more or less cofounded by HCA in a different way:

- Seroprevalence surveys and hospitalizations by supply HCA.
- Document case notifications and crude mortality rates by demand HCA.

Moderating role of HCA could be changing in time; however, this simple analysis suggests that including HCA indexes into models of disease dynamics could increase their predictive power. Moreover, recent suggestions of ECDC [22] and WHO [23] to put more emphasis on hospitalizations/mortality rather than laboratory confirmed cases in understanding the burden of disease is supported by our findings too. Moreover, the lack of or even slightly positive correlations between current incidence and vaccination rates by regions has been confirmed in our study to be significantly confounded by HCA. As this argument is often used by antivaxx movement, it is worth to mention that causal relation cannot be claimed with the observed moderating role of HCA. Thus, vaccination is not only averting hospitalization [20] or death tolls [24] in Poland (Fig. 2, 4), but also probably reduced transmission probability, although it may be partially masked by inequalities in HCA (Fig. 3).

This study is only an exploratory, so-called "zero" approach to illustrate the mediating phenomenon of HCA and has multiple limitations because vaccination coverage, cumulative case notifications, seroprevalence and current outbreak dynamics have been taken for different time periods. Due to availability of explained variables on different levels (voivodeship or poviat) model comparison should be done with caution. Other possible interfering variables were not taken into consideration (as socio-economic-demographic picture of the population). We regret that data gathered by state is not provided in an easy to analyse format [25] and massive manual work is needed for data preparation. The most important variable – hospitalization – is not available on poviat level (old NUTS-4). We suggest that the number of hospitalized patients originating from a given region (poviat) could be a very important epidemiological index. Further causal modelling using a longitudinal approach is required to support our preliminary observations. These results are specific to the Polish population / healthcare system and the role of the access to healthcare could be different in other settings.

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