

What Matters among Non-pharmaceutical Interventions on COVID-19 in Europe?

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Abstract

Objectives

The purpose of this study is to describe the situation of the COVID-19 in European countries and identify important factors related to prevention and control.

Methods

We obtained data from World Health Statistics 2020 and the Institute for Health Metrics and Evaluation (IHME). We calculated the R_t values of 51 countries in Europe under different prevention and control measures. We used lasso regression to screen factors associated with morbidity and mortality. For variables selected, we used quantile regression to analyze the relevant influencing factors in countries with different levels of morbidity or mortality.

Results

The government has a great influence on the change of R_t value through prevention and control measures. The most important factor for personal and group prevention and control is the mobility index, testing, the closure of educational facilities, restrictions on large-scale gatherings, and commercial restrictions. The number of ICU beds and doctors in medical resources are also key factors. Basic sanitation facilities, such as the proportion of safe drinking water, also have an impact on the COVID-19 epidemic.

Conclusions

This study describes the current status of COVID-19 in European countries. We found key factors in individual prevention and control measures and group prevention and control measures.

Background

Due to December 7, 2020, there have been 66,243,918 cumulative cases and 1,528,984 cumulative deaths worldwide according to WHO's data on Coronavirus Disease (COVID-19). The WHO announced that COVID-19 has developed into a pandemic on March 12, 2020, which is defined as a global public health emergency of high international concern. The COVID-19 is an acute respiratory infectious disease transmitted mainly through aerosol and droplets¹. The COVID-19 is characterized by higher infectivity than SARS, but the mortality rate was lower, so we should strengthen the prevention and control of COVID-19².

Many countries have taken some restrictive measures to control the infection. The main measures include case isolation and medical surveillance of close contacts. Before the large-scale use of vaccines, the main non-pharmacological prevention and control measures mainly included individual prevention and group prevention. Personal prevention and control mainly include wearing masks, washing hands, proper social distance, and reducing outdoor activities. Group prevention and control mainly include travel restrictions, home isolation,

closure of educational facilities, prohibition of public gatherings, all commercial activities and non-essential commercial activities. The effect of prevention and control may also be related to medical resources, such as doctors, nurses, pharmacists, ventilators, ordinary beds, and ICU beds. The country's economic situation and ability to respond to public health incidents. For example, GDP and GHS may be related to the effectiveness of prevention and control.

The World Health Organization recommends a variety of measures: rapid diagnosis and immediate isolation of cases, strict tracking and preventive self-isolation. Switzerland regards testing as the main method to control COVID-19³. Widespread testing for COVID-19 will draw a clear picture of the dynamic of the COVID-19 epidemic. Without clear numbers, it will be very difficult to evaluate whether control measures were effective. A meta analysis showed that medical masks and N95 masks can protect against viral respiratory infection including coronavirus⁴. Community-wide mask wearing can contribute to the control of COVID-19 by preventing contact with large amounts of saliva and respiratory droplets from asymptomatic COVID-19 patients⁵. Hand hygiene is the most important factors of control activities and infection prevention because it reduces the quantity of microorganisms on your hands and minimizes the possibility of transmission to other people⁶. The use of antiseptic hand soaps offered a greater reduction in the number of microorganisms compared with regular soaps⁷. However, toxicity and stability of surface disinfectants, are the issues that should be further investigated⁸. Governments have advocated by implementing physical distancing and self-isolation and reducing outdoor activities in many countries. The findings of a systematic review and meta-analysis support that physical distancing of 1 m, face masks, and eye protection to prevent person-to-person transmission of COVID-19, Which ones are relevant to the best evidence currently available and can be used for interim guidance. The randomized control trials are needed to better inform the evidence for these interventions⁹.

The first country in Europe where the COVID-19 outbreak was Italy. On 9 March 2020, the Italian government implemented a comprehensive "blockade" policy, mainly consisting of travel restrictions, mandatory staying at home (except for health problems, emergencies or regulated shopping for necessities) and temporary closure of nonessential businesses and shops, which lasted until 3 May 2020. In the following months, many European countries also adopted similar measures¹⁰. In March 2020, 47 countries did not allow commercial flights to land. This can stop the development of this virus, but we should work together¹¹. What's more, It is necessary to develop an international framework that outlines the method, time and scale of travel restrictions according to the stage of the epidemic¹². A cross-sectional study suggests that issuing a stay-at-home ban may help limit the spread of COVID-19 cases in Iowa¹³. On March 12, Norway issued stricter measures and instituted quarantine for those who entered the country. The same day, the government closed all schools and kindergartens, psychologists, physiotherapists, hairdressers, psychologists training centers and swimming pools, forbided cultural and sporting events. Sweden chose a different strategy: kindergartens, elementary schools, other businesses and training facilities continue to open, and children's sports continue¹⁴. Mass gatherings are related to the high transmission rate of SARS-CoV-2, and many sporting events have been restricted or canceled to limit disease spread¹⁵. Some non-essential business such as vape shop were closed¹⁶.

The disease incidence, daily cumulative index, mortality of COVID-19 were related to country healthcare resources and economic status¹⁷. In Italy, 16% of hospitalized COVID-19 patients require intensive care. Compared with Germany, the medical resources in northern Italy are overwhelmed by the increase in patients. In

contrast, Germany has a wider distribution of cases and can make better use of resources. For every 100,000 population, Germany has more intensive care beds than Italy. The high mortality rate in Italy may reflect the relationship between the availability of medical resources and outcomes¹⁸. In addition, the prevention and control effect of COVID-19 may be related to indications such as GDP(Gross Domestic Product)and GHS(Global Health Security Index)¹⁹.

Materials And Methods

Research objective and data sources

We obtained data from World Health Statistics 2020 and the Institute for Health Metrics and Evaluation (IHME). The IHME is an independent population health research center at University of Washington Medicine, part of the University of Washington, that provides rigorous and comparable measurement of the world's most important health problems and evaluates the strategies used to address them. We selected 51 countries in Europe as our research objective. There are 53 countries in Europe according to WHO regional groupings. The data of Monaco and Turkmenistan is incomplete, so we discarded these two countries. Where does IHME obtain its data? These forecasts include data from local and national governments, hospital networks and associations, the World Health Organization, third-party aggregators, and a range of other sources.

For testing data, IHME rely primarily on data reported by Our World in Data. However, for Cyprus, Italy and Spain, they used government data. IHME obtain hospital resource data from sources such as government websites, hospital associations, the Organisation for Economic Co-operation and Development, WHO, and published studies. For population density, They used gridded population count estimates for 2020 at the 1 x 1 kilometer (km) level from WorldPop. For mobility index data, IHME used anonymized, aggregated data from Google, Facebook, and Apple. Their data on mask use come from Premise, Facebook Global Symptom Survey (research based on survey results from the University of Maryland Social Data Science Center), Kaiser Family Foundation (KFF), and YouGov COVID-19 Behaviour Tracker survey.

Statistical Analysis Method

We described the changes in the R_t values of 51 European countries under different prevention and control measures. We also analyzed and evaluated the prevention and control effects of COVID-19 in European countries. We used Lasso regression to screen factors related to morbidity and mortality. For the selected variables, we used quantile regression to analyze relevant influencing factors in countries with different morbidity or mortality.

Changes of R_t under different prevention and control measures

There are roughly four methods for estimating R_t , exponential growth method, maximum likelihood method, sequential Bayes method, and time-dependent basic regeneration number method. In this study, we used the time-dependent basic reproduction number method, and we mainly focused on the time-dependent reproduction number (R_t). R_t is the average number of secondary cases of a single infected person during the t day of infection. R_t is usually used to describe the transmission characteristics of pathogens during a disease epidemic, and it can also evaluate the effectiveness of interventions. When R_t is greater than 1, it indicates that

the number of infections is increasing rapidly; when R_t is less than 1 and close to 0, it indicates that the epidemic has been effectively controlled²⁰.

Lasso Regression

Two methods of variable selection in linear regression model mainly include subset selection method and coefficient compression method. The traditional linear regression method belongs to subset selection method and the main method to screen variables is the least square(OLS) method. However, this method has some defects: variable selection is separated from model parameter estimation, so the model error increases; Small changes of variables have great influence on variable selection. Variable selection is not suitable for high dimensional data^{21,22}. With the booming field of machine learning, there has been growing number of statistical tools compensate for the limitations of traditional methods. The least absolute shrinkage and selection operator regression (lasso regression) is the representative regularization method can effectively optimize OLS estimation and treatment Overfitting problem²³. By introducing penalty term into model estimation, Lasso method can obtain higher prediction accuracy and model generalization ability. It also can effectively deal with overfitting and multicollinearity problems²⁴⁻²⁶. The specific formula can be expressed as:

$$\hat{\beta}(\text{lasso}) = \arg \min_{\beta} \left\| \mathbf{y} - \sum_{j=1}^p \mathbf{x}_j \beta_j \right\|^2 + \lambda \sum_{j=1}^p |\beta_j|.$$

The first part represents the standard OLS loss function, the second part represents the penalty function. It represents the tuning parameter for controlling the degree of regression coefficient compression, when λ is ≥ 0 . the greater the value, the stronger the penalty will be. When $\lambda=0$, The loss function does not penalize the model. Lasso regression shrinks some coefficients and sets others to 0 and tries to retain the good features of both subset selection and ridge regression²⁷. Researchers adopt different forms of penalty functions according to the different characteristics of independent variables in regression analysis on the basis of Lasso. Many kinds of regularization models have been established and developed, such as Relaxed Lasso²⁸, Adaptive Lasso²⁶, Bayesian Lasso²⁹, Fused Lasso²⁴ and Group Lasso³⁰ and elastic net²⁵ etc.

Quantile Regression

Quantile regression (QR) is a method of estimating the linear relationship between the different quantiles of the dependent variable and the independent variable. Both QR and original linear regression (OLS) can be seen as solutions to specific minimization problems. The estimation of OLS regression is based on the smallest residual square, and the estimation of QR is based on the smallest weighted absolute value residual. The minimum weighted absolute deviation of quantile regression is as follows:

$$\min \{w_{\tau} |y_t - \alpha|\} = - \sum_{i:y_i < \alpha}^T (1 - \tau) (y_t - \alpha) + \sum_{i:y_i \geq \alpha}^T \tau (y_t - \alpha)$$

The essence of quantile regression is to calculate the regression coefficients of different quantile values of the dependent variable. It can comprehensively display all data information to a certain extent, but it focuses more on the overall heterogeneity analysis of features distributed in different locations. It can not only measure the influence of regression variables in the center of the distribution, but also the influence on the upper and lower tails of the distribution. Therefore, it has unique advantages over traditional linear regression models and can obtain comprehensive analysis results. Especially for the condition of uneven distribution, quantile regression is more comprehensive and accurate than traditional linear regression coefficient estimation³¹.

Results

Our results are divided into 3 parts. First, we calculated the changes in R_t under different prevention and control measures. Secondly, lasso regression screened 17 variables that were relative to cumulative mortality and cumulative morbidity, and finally lasso regression screened out meaningful variables for quantile regression. We explored the impact of various variables at different levels of morbidity and mortality. R software 4.0.2 and stata15.0 are used for all our statistical analysis.

Changes of R_t under different prevention and control measures

We have plotted the changes in R_t values of 51 countries in Europe. After an outbreak period ranging from 2–3 months, the R_t of France, Denmark, Belgium, Armenia, Germany, Netherlands, Spain, Portugal, Moldova, Sweden, Tajikistan, Turkey, Uzbekistan are basically stable, the value fluctuates around 1. Russia and Ukraine have a longer outbreak period, but the R_t afterwards also stabilized at around 1. The R_t of other countries fluctuates to varying degrees. The general trend of changes of R_t in the most European countries, which were showing an increasing trend after October and have exceeded 1.

Let's take Finland and Switzerland as examples. In Fig. 1A, we describe the changes of R_t value in Finland under different prevention and control measures. The first case of COVID-19 occurred in Finland on January 28, and on March 18, any business activities were banned and educational facilities were closed. Travel restrictions has be implemented on March 25, and unnecessary business activities has be prohibited on April 4. The prevention and control effects have been achieved and the R_t value has dropped below 1, under the above four powerful group interventions. On May 29th, the government ended travel restrictions. On June 1, the government ended the ban on restricting any business activities and restricting non-essential commercial activities. Due to the relaxation of the intervention policy, the R_t value rebounded and rose. On July 24, R_t value reached a small peak of 3.296. On August 13, when the R_t value dropped to 1.398, the restriction on school facilities closure was ended. Then on October 11, the R_t value fluctuated repeatedly, and on October 11, it reached 1.966.

In Fig. 1B, we describe the changes of R_t values in Switzerland under different prevention and control measures. Cases appeared in Switzerland on February 23 and large gatherings were banned on February 28. On March 13, the education facilities were closed. On March 16, any commercial activities and non-essential commercial activities have be prohibited. Under the above group intervention, a certain prevention and control effect was achieved and the R_t value dropped below 1. Thus, on April 27, the government ended the restrictions on non-essential commercial activities. On June 6, the government ended the ban on any commercial activities. On June 8, the government decided to end the closure of school education facilities. Due to the relaxation of the intervention policy, the R_t value rebounded and rose. On July 2, the R_t value appeared a small peak of 2.88.

Subsequently, the R_t value dropped to around 1. On October 16, there was a small peak of 2.51. The graphs of R_t changes in other countries can be seen in the supplement materials.

Result of Lasso Regression

In this study, the relationship between 2 dependent variables and 17 independent variables was explored, including cumulative morbidity (Y1) and cumulative mortality (Y2). The independent variables are density of medical doctors/per 10 000 population(X1), density of medical nursing and midwifery personnel/per 10 000 population(X2), Density of medical pharmacists/per 10 000 population(X3), GDP per capita(U.S. dollars per capita)(X4), proportion of population using safely -managed drinking-water services (X5),total test(X6), mask use rate(X7), mobility composite (X8), excess bed capacity for COVID-19(X9),ICU excess bed capacity for COVID-19(X10),travel restrictions(X11),stay at home(X12),educational facilities closed(X13), any gathering restrictions(X14), Any business closures(X15), Non-essential businesses ordered to close (X16), Global Health Security index(X17).

5 variables were finally screened out of 17 variables related to cumulative morbidity(Y1) and 7 variables related to cumulative mortality(Y2), after lasso regression selection. The specific content is shown in Fig. 2. We can see that when the average mean-squared error is the smallest, lasso regression screens out 5 variables in Fig. 2A, at this time $\lambda = 0.09559$. Among them, the selected variables are X1(density of medical doctors/per 10 000 population), X5 (Proportion of population using safely -managed drinking-water services), X8 (mobility composite), X14 (any gathering restrictions), X16(Non-essential businesses ordered to close). We can see that when the average mean-squared error is the smallest, lasso regression screens out 7 variables in Fig. 2B, at this time $\lambda = 0.0822$. Among them, the selected variables are X5 (Proportion of population using safely -managed drinking-water services), X6(total test), X8 (mobility composite), X10(ICU excess bed capacity for COVID-19), X13(educational facilities closed), X14 (any gathering restrictions), X16(Non-essential businesses ordered to close). The selected indicators were closely related to cumulative morbidity and mortality.

Results of the Quantile Regression

The results of quantile regression are different from the results of lasso regression, and quantile regression provides more comprehensive information. The specific content is presented in Table 1. The changes of coefficients and confidence intervals in quantile regression are shown in Fig. 3. The overall result is that the mobility index, the ratio of safe drinking water, and the closure of non-essential businesses are related to the cumulative incidence. Educational facilities closed, any gathering restrictions, Non-essential businesses close are related to cumulative mortality. In low- and medium-incidence countries, the total number of tests is related to the cumulative incidence. In high-incidence countries, closed educational facilities and any gathering restrictions are related to cumulative mortality.

Discussion

Our study found that the population prevention and control measures implemented by the government had an impact on the change of R_t value. In most countries, the R_t value has a clear upward trend in October. The most important factor in personal prevention and control is the mobility index. Group prevention and control on the total testing, closure of educational facilities, restrictions on large-scale gatherings, commercial restrictions and other government interventions are very important for prevention and control. The number of ICU beds and the

average number of doctors in medical resources are also key elements. Basic sanitation, such as the proportion of safe drinking water, also has a certain impact on the COVID-19 epidemic.

The rate of masks using in individual prevention has not been found to be related to cumulative mortality or morbidity. It does not mean that the use of masks has no effect on prevention and control. Research on the effectiveness of masks for prevention and control has been confirmed⁴. The lasso regression finds variables with a very large degree of correlation, so the mobility index generated by personal behavior in the movement of personal behavior in prevention and control may be more important than wearing a mask. Secondly, we think the possible reason is that the data on the rate using of masks comes from social surveys and there may be large errors.

Some studies have reached conclusions consistent with ours. The results of the dynamic SEIR model show that the lockdown control measures implemented by China on January 23, 2020 are essential to ultimately reduce the scale of the COVID-19 epidemic³². A study found that the effectiveness of different interventions varies. They estimated that early detection and isolation of cases prevented more infections than restrictions on travel and reduced contact. Non-drug interventions should be combined to achieve rapid results. Our research also found that there is a certain relationship between cumulative mortality and testing³³. Some scholars even proposed that the best strategy is to use both robot recognition and migration restriction strategies. In China, robots are assigned multiple tasks to minimize the spread of COVID-19, such as using them to clean and prepare food in epidemic areas that are harmful to humans. European countries can also take this approach to reduce exposure to infection and provide help for the prevention and control of diseases³⁴. Once the initial pandemic is under control, we must turn our attention to how to improve the adverse effects of the lockdown³⁵.

Studies have also shown that medical resources are related to the mortality rate of COVID-19, which is close to our research conclusions. We have found that the number of doctors per capita and the number of hospital beds per capita are related to the incidence or death of COVID-19³⁶. The experience in Wuhan suggests that if the medical resources become scarce, the government should establish temporary hospitals and Medical staff will be deployed from areas where the epidemic is relatively mild to ease the pressure in severely affected areas. Effective quarantine via quick detection prevent a larger outbreak^{37,38}. It is necessary to establish medically necessary, time-sensitive procedures scoring system during the COVID-19 Pandemic³⁹. Within days or weeks, the health system is reorganized. We must optimize health resources. Fight for disease in a joint medical team composed of doctors, nurses, pharmacists, and respiratory therapists⁴⁰.

The ratio of safe drinking water in basic health resources has a certain relationship with the cumulative morbidity and mortality of COVID-19, which may be related to the fact that hand washing can reduce the number of hand viruses and achieve a certain prevention and control effect. Basic cleaning services are a basic prerequisite for compliance with the principles of infection prevention and control, which are necessary to protect patients, health workers and susceptible people⁴¹.

Some indicators, such as nurses per capita, pharmacists per capita, GDP and GHS, are not included in the regression model, which may be due to the relatively low correlation degree. After the Ebola outbreak in 2014, the Global Health Security Index (GHSI) was developed to measure the ability of countries to respond to infectious disease outbreaks. Six core elements were evaluated: prevention, detection and reporting, response,

health system, compliance with norms and the risk of infectious disease outbreaks. The score higher of GHSI, the better the preparation.

Studies have shown that GHSI and JEE (Joint External Evaluation) have low predictive value for the death outcome of COVID-19, and we have reached the same conclusion^{42,43}. For example, UK, which ranks second in GHSI score, also bears a huge burden of disease⁴⁴. However, some studies have shown that GHSI has a predictive effect on the burden of COVID-19, but in the opposite direction⁴⁵.

Our research has some advantages. First, this study describes the prevalence and control of COVID-19 in European countries and the workload is relatively large. Secondly, this study included many independent variables to analyze their relationship with dependent variables. The independent variables mainly include individual prevention and control, group prevention and control, medical resources, basic health facilities, and comprehensive indicators. Thirdly, this paper uses lasso regression to screen variables with a smaller error than traditional regression and the results are more accurate. Quantile regression is further used to quantify the specific situation of each divided point, which provides more information than traditional regression. Of course, our article also has some shortcomings. For example, a small number of proven effective prevention and control measures have not entered our regression model, which may be related to the accuracy of the data and the impact of variables.

Conclusions

This study comprehensively describes the current status of COVID-19 prevention and control in European countries. We found key factors in individual prevention and control measures and group prevention and control measures, which can provide a policy basis for the prevention and control of epidemics in European countries.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

YL acquired the data, performed the analysis of data, and wrote the manuscript. QY and HW acquired the data and contributed to the analysis of data. FS, FW and YZ contributed to the coding of the statistical analysis. CY evaluated the whole work.

All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 Results of the Quantile Regression

Quantiles		0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
Y1	(Intercept)	-3.88	-1.35	-14.06	-8.92	-11.81	-27.89	-25.56	-27.45	-3.62
	X1	0.12	0.05	0.11	0.01	0.18	0.10	0.01	-0.01	0.46
	X5	0.04	0.07*	0.16*	0.17*	0.10*	0.31*	0.32*	0.35	0.31
	X8	-0.21	-0.09	-0.44	-0.42*	-0.52*	-0.52	-0.69	-0.68	-0.51
	X14	-2.73	-3.36	-4.67	-5.39	-4.26	2.12	-0.39	-0.20	-28.64
	X16	4.32	6.44*	5.12*	5.15*	8.30*	6.51*	8.81*	12.12	17.33
Y2	(Intercept)	-8.54	-14.20	0.79	-8.84	35.08	15.56	-22.43	-17.87	-111.83
	X5	0.08	0.01	-0.04	0.09	0.19	0.23	0.54	0.74	1.44
	X6	0.00	0.00	0.01	0.01	0.00	0.00	0.00	-0.01	0.00
	X8	-0.30	-0.69	-1.09*	-0.86	-0.82*	-1.28*	-1.74*	-1.47*	-2.60*
	X10	7.46	5.64	1.78	0.15	4.52	8.27	-4.70	-15.30	-33.26
	X13	3.83	-7.50	-57.16	-51.27	-48.17	-44.13	-31.18	-20.35*	8.17
	X14	-6.59	7.77	39.84	41.69	-10.86	-6.85	1.25	-14.87*	5.63
	X16	3.87	10.08*	13.73*	12.66*	16.70*	21.59*	19.06*	25.98	1.94

* indicates that the coefficient is statistically significant

Figures

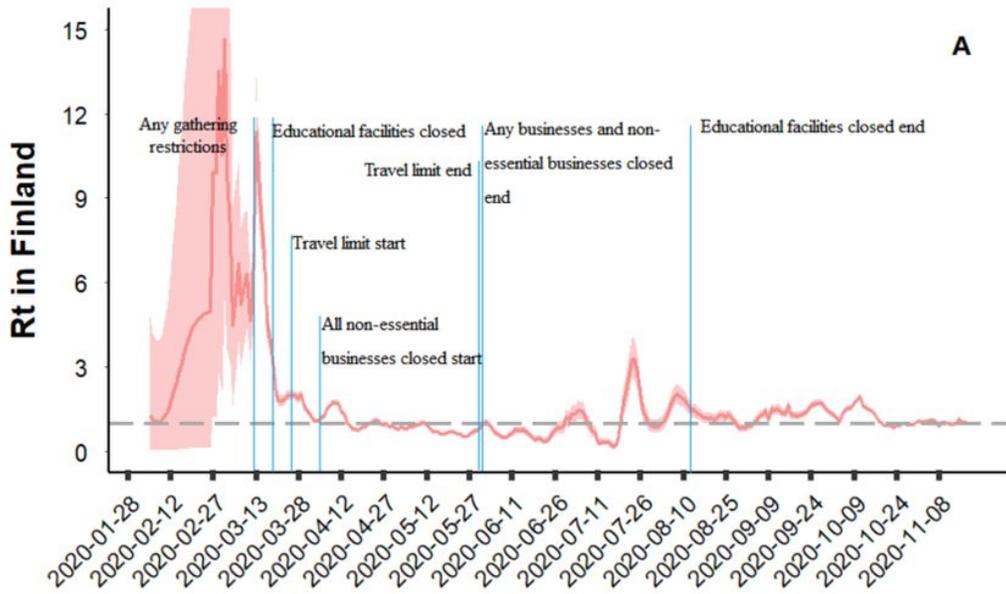


Figure 1A Changes of Rt in Finland under different prevention

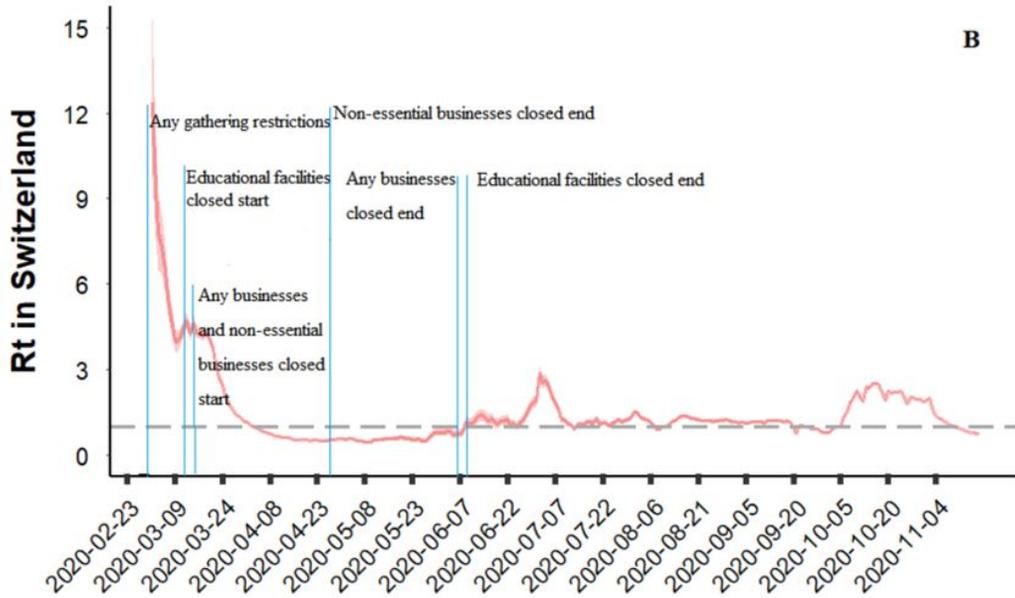


Figure 1B Changes of Rt in Switzerland under different prevention and control measures

Figure 1

A Changes of Rt in Finland under different prevention. B Changes of Rt in Switzerland under different prevention and control measures

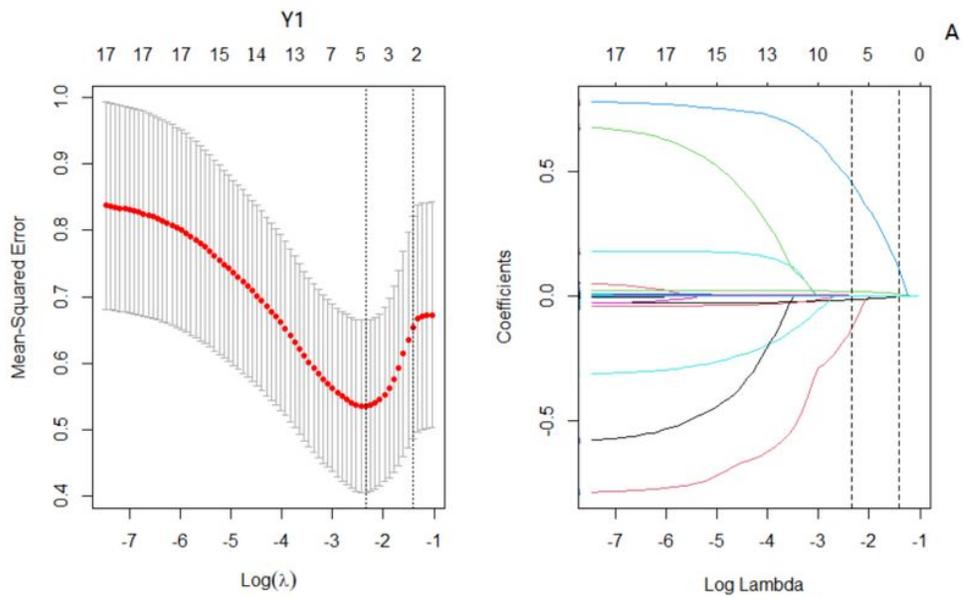


Figure 2 A The process of selecting variables in Lasso regression

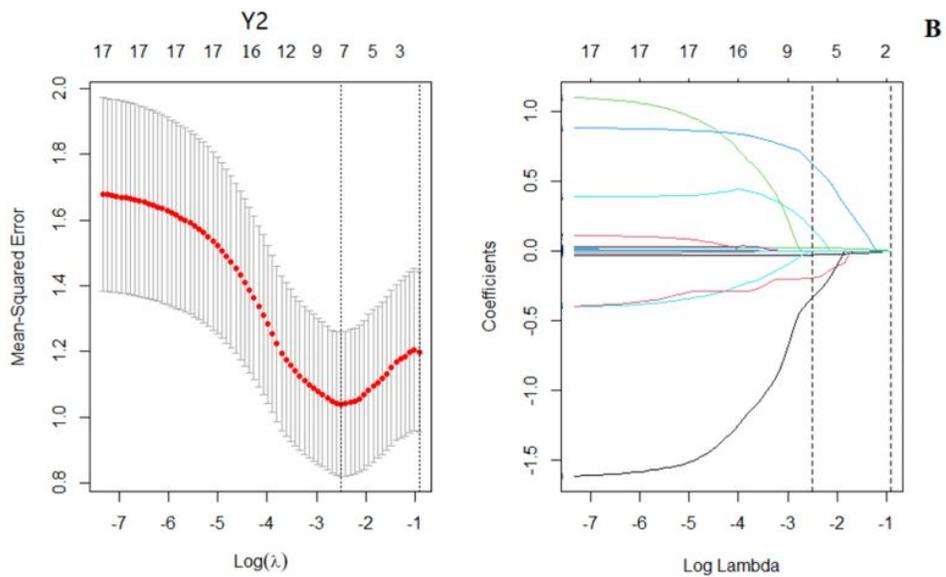


Figure 2 B The process of selecting variables in Lasso regression

Figure 2

A The process of selecting variables in Lasso regression. B The process of selecting variables in Lasso regression

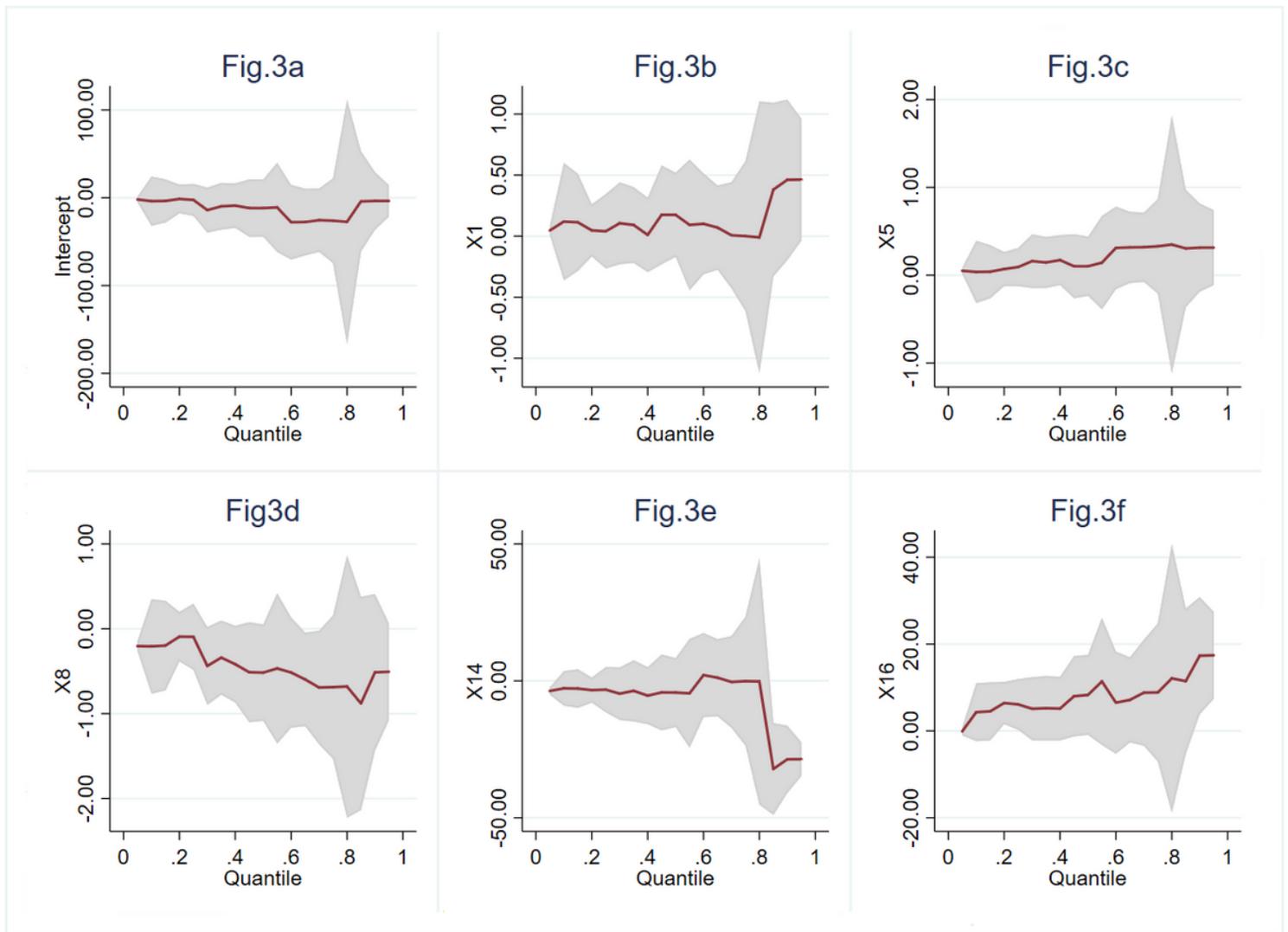


Figure 3

The changes of coefficients and confidence intervals in quantile regression β_{Y1}

Supplementary Files

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