

Report

Correlation of Influenza Vaccination and Influenza Incidence on Covid-19 Severity

Mark Christopher Arokiaraj, MD DM,

Cardiology, Pondicherry Institute of Medical Sciences,

India 605014.

christomark@gmail.com

Key words: Covid-19, Influenza vaccination, Influenza lower respiratory tract infections, Mortality, Morbidity, Immunity.

Abstract

The pandemic of Covid-19 is evolving worldwide, and it is associated with high mortality and morbidity. There is a growing need to discuss the elements of coordinated strategy to control the spread and mitigate the severity and mortality of Covid-19. H1N1 vaccine and streptococcus pneumonia vaccines are available. The current analysis was performed to correlate the severity of Covid-19 and influenza (H1N1) vaccination statistics and also the influenza lower respiratory tract incidence. There is a correlation between Covid-19 related mortality and morbidity and the status of influenza vaccination, which appears protective. The tendency of correlation is more visualized as the pandemic is evolving. The case incidence and recovery parameters also showed a beneficial trend. Since evolutionarily influenza is close to SARS-CoV-2 viruses and shares some common epitopes and mechanisms, there is a possibility of partial protection to reduce the Covid-19 related severity using the influenza vaccination. In countries where influenza immunization is less, there is a correlation between lower respiratory tract infections (LRI) and influenza attributable to lower respiratory tract infections incidence and Covid-19 severity, which is beneficial. Receiver operating curve (ROC) statistics showed an area under the curve of 0.86 (CI 0.78 to 0.944, $P < 0.0001$) to predict Covid-19 mortality >150 /million, and a decreasing trend of influenza LRI episodes. Influenza (H1N1) vaccination is cost-effective and safe.

Influenza vaccination (H1N1)

The influenza viruses and SARS-CoV-2 viruses have evolutionary proximity. The influenza and coronaviruses utilise similar and contrasting approaches to control interferon stimulated gene responses.¹ Also, the pathognomonic spike protein shares common features with class 1 viral membrane fusion protein including influenza viruses.^{2,3} The cell entry of the influenza A (H7N9) viruses is through ACE-2 receptors in the lung.⁴ The exact receptor mechanism of the virus entry is still not clear, however, the surface hemagglutinin receptor binding sites attaches the virus to surface glycoconjugates that contain terminal sialic acid residues.^{5,6} H1N1 infections can downregulate the ACE-2 levels in the lung tissues by neuraminidase.⁷ Hence, the study was performed to analyse the severity of Covid-19 and influenza vaccination in adults >65years. Since this vaccination is not mandatory for routine clinical practice, various countries adopt different policies, and the vaccination rates significantly differ among various countries.

The influenza vaccination status data in the elderly >65years was obtained from OECD (organisation for economic cooperation and development) data,⁸ and the data of countries that are not available in the OECD data were obtained from various publications.⁹⁻¹³ At the time of this writing, the details of the Covid-19 were obtained from worldometer data/coronavirus and the current mortality worldwide is 550 000. The number of critical or the severe nature of the patients were obtained from the same source. The critical or the severe patients were compared with the respective population of the countries.

Case incidence

Table 1 shows the statistical data from the worldometer data/coronavirus at the time of this write up. The correlation between vaccination and cases per million/vaccination shows an R_2 of 0.16 and a variance benefit of 15 percent (Figure1). When adjusted to the tests performed which modulate the case identification, the benefit is more pronounced, and R_2 was 0.28 ($r = -0.53$, Figure 1 Panel C) and is sustained around 0.26 (Panel E, Figure 1). The latest R_2 was 0.15 (Panel F lower line, Logarithmic R_2 0.26). There is a tendency of lesser case incidence in vaccinated countries.

Mortality

There was a statistical correlation between the influenza vaccination status and the mortality of the Covid-19 illness (Figure 2, Panels A to H). The latest R_2 was 0.01 and logarithmic R_2

was 0.0937 (Figure 2, Panel H). The correlation graph shows vaccination status and mortality reduction. When the mortality figures were adjusted to the case numbers/million population, then the mortality benefit was significant (Figure 3, Panels A to I). Correlation graphs showed a variance of about 25 to 34.6% towards mortality benefit. The latest R^2 value July 4, 2020 was 0.338 (Figure 3 - Panel I upper line), and the logarithmic R^2 was 0.416. Though it is not a traditional $R^2 > 0.7$, there are many parameters affecting mortality. Since mortality is a major end point, and it can be affected by various parameters pertaining to baseline characteristics, clinical and demographic variations the variance benefit by immunisation alone is significant. Hence, the results in figure 3 correlation have a contribution to mortality reduction. A correlation between vaccination and mortality/cases per-million adjusted to population (figure 4) showed a R^2 0.13 ($r = -0.367$) to 0.14. When it was further adjusted to the tests performed the R^2 was about 0.09 to 0.1 (figure 4, Panels B and C).

Some countries have differences in their testing strategy, and therefore the results were further adjusted with tests performed/million population. The correlation was performed after correction for tests performed/million people in the next figure 5 (Table2). The vaccination parameter after correction for tests performed/million showed a variance of 23.3 percent (r^2 , figure 5 Panel A; April 15-2020), which increased to 25.9 percent (figure 5 panel B; April 20, 2020), thereafter to 29.1 (figure 5 Panel C; April 25, 2020) and the recent values are 30.2 percent ($r = -0.55$, Panel E, May 18 2020) and 29.3 percent (Panel F, May 31, 2020). There is also a tendency for more correlation as the pandemic is evolving. When the tests performed were used as a divisor instead of multiplication, the R -value was about 0.16 ($r = -0.4$, Figure 6) and the latest being 0.176 (May 31,2020 - Figure 6). The multiplication technique reflects the magnitude of the problem and the effect of vaccination. The divisor technique demonstrates the impact of the quality of care and the modulation of immunization on mortality. Therefore, both methods are useful for analysis. When the death per million/cases per million parameters was adjusted with concerned countries population, the R^2 -value ranged from 0.26 ($r = -0.51$) to 0.3 ($r = -0.55$).

There were few countries with a small population that did not show the correlation. A search was performed to analyse the incidence of influenza in countries which did not show correlation. Among the countries studied, Latvia, Serbia, Slovak, Turkey, Slovenia, Czech Republic, and Slovenia were the countries that showed no correlation with vaccine status. In these countries, incidence if flu is more and it is perennial i.e., throughout the year than the

seasonal pattern seen in other countries like Spain, Italy, Belgium, Netherlands, Sweden, Scotland, and Luxembourg.¹⁴ The incidence of influenza in Turkey and neighbouring countries recently was high.¹⁵ Also, different countries are in the various stages of disease presentation and spread, and hence they can differ in mortality statistics.

The central, eastern European and Central Asian countries have a high incidence of lower respiratory tract infections (LRI), which are 41.4/1000, 81.2/1000, and 58.5/1000 compared to the high-income northern America (38.8/1000) and western Europe (28.7/1000).¹⁶ In the elderly population, the statistical numbers for LRI are 120/1000, 203/1000 and 168.5/1000 are respectively for central, eastern European and central Asian countries when compared to high income 73.2/1000 in north America and 101/1000 in western Europe. Analysing the children (<5 years) data who play an essential role in herd immunity the high-income nations the incidence of LRI in children, which is about 44.6/1000, Central and Eastern European countries have 107/1000, and Asian countries have an incidence of 120/1000. Hence, in the eastern European and central Asian countries have higher LRI episodes and lesser Covid-19 deaths. This includes Russia which is classified under Eastern European countries. Similarly, Turkey, which is classified under North Africa and Middle East countries, has overall LRI episodes of 56.5/1000, and in the children population, it is 133.2/1000, and in the elderly, the incidence is 246/1000.¹⁶

South Korea has the highest vaccination rates of 82.7 percent in elderly vaccination (>65years) and had an early incidence of the pandemic, has the least mortality compared to the early onset countries (worldometer data). Some of South Korea's past data showed influenza vaccination rates up to 86% in the elderly (>65yrs).¹⁷

In the US adult (>18 years) vaccination rates were higher in states like North Carolina, Washington, Iowa, Maryland, Connecticut and Massachusetts areas, with a mean vaccination rate of 52%.¹⁸ The mortality burden is lower in these states compared to other states within US, where the mean vaccination rate was about 47%. Neighbouring countries with similar climatic conditions like Belgium and the Netherlands have variations in mortality i.e., 843/million and 357/million, respectively. The vaccination status in the elderly (>65 years) differ between Belgium and the Netherlands, which is approximately 31 and 64 percent, respectively.

Closed cohorts – US military, Diamond Princess and Ruby Princess

Data from the US military cohort shows an incidence of coronavirus cases of 18 071 cases, and the mortality was 38 cases to date. The case-fatality ratio is 0.21 percent, which is the least. Age distribution of the mortality statistics is not available for further analysis. The military personnel are known for regular vaccination schedules, including influenza, streptococcus pneumonia, and Haemophilus influenza, and this can represent useful data.¹⁹ Better nutrition and physical health status also add to their outcome. US veteran's affairs Covid-19 worldometer data shows mortality of 1678 out of 24 394 cases with a case fatality of 6.8 percent. However, advanced age and more comorbidities like diabetes, etc. would be associated, and the vaccination for influenza was about 71 to 75%, and in some subgroups, it extends to 82%.²⁰

The cruise ship Diamond Princess represents another closed cohort, and the vaccination details are not available. Nevertheless, the average vaccination statistics can be assumed to be 50%, since the average adult (>18years) US data for vaccination is 48%, and Scotland has an average of 50%.²¹ The total members on board including crew was 3711. Seven hundred twelve cases of Covid-19 were reported, and the mortality of about 13 cases to date and seven patients are serious or critically ill.²² However, a head-to-head comparison is not feasible as the population in Diamond princess with > 70 age was 1230 out of the total 3711, and the mean age was 58 years. The case-fatality ratio is 1.8 percent; however, it could be higher as the details of patients repatriated to various countries after dis-embarkment is not available. The other cruise ship Ruby princess had an incidence of 686, and the mortality number was 21 patients till now.²³ The case-fatality ratio was three percent. Other cruise ships like MS Zaandam (Holland-America) reported fewer case numbers, and hence, it was not taken for analysis.

In the US, among the health care workers, the influenza vaccination rates are about 81%. In particular, physicians (96.7%) and nurses (98.1%) have very high vaccine uptake rates.²⁴ Whereas among other allied health care professionals, the vaccine uptake rate ranges from 75 to 85%. So far, the incidence among health care workers was 92 572, and the mortality was 507 cases which is 0.54 percent (<1 percent).²⁵

Antibody testing, when performed in New York, showed about 20% of the population developing antibodies.²⁶ Similar tests performed in Sweden reveals antibody levels of about 7.3% with highest levels in Stockholm and maximal antibody levels were seen in the age group

20 to 64 years.²⁷ In both instances, the tests were performed in a limited number of subjects i.e., 3000 and 1200 subjects, respectively. Tegnell's method of limited lockdown in Sweden, though it has higher mortality in the initial stages of coronavirus pandemic, can benefit more with supplementation of the H1N1 vaccine in the age group 20 to 64 years and enhancing in the elderly. The exact benefit of this method can be quantified as a comparison, only when other countries ease the lockdown measures. The other Scandinavian countries can administer H1N1 vaccination in the adult population, which can reduce mortality as most countries aim to reduce lockdown.

The case numbers are increasing, and at present, the incidence of Covid-19 is 11.5M, all over the world. Yet a vast majority of the world's population is not affected. As the lockdown measures are relaxed the incidence and mortality of Covid-19 would increase. Till a herd immunity is achieved, which is at least 60% of people being infected, the pandemic effects will be seen. The foresight for a dedicated vaccine would be at least 6m from now. SARS-CoV-2 is an evasive candidate for vaccine development, and a pandemic of RNA virus was predicted by the scientists in 2017.²⁸

A recent study²⁹ has observed a positive correlation between influenza vaccination and Covid-19 mortality in Europe ($r = 0.68$ and $R_2 = 0.46$), and in US ($r = 0.29$, and $R_2 = 0.084$). Also, in that study, there was a mild correlation in the case fatality ratio with vaccination in Europe ($r = 0.38$ and $R_2 = 0.14$). There was no correlation in the case fatality rate in the US ($r = 0.19$ and $R_2 = 0.036$). The study includes more eastern European countries with low vaccination rates – Romania, Cyprus, Malta, Bulgaria, Greece, and Poland. Whereas, the current paper includes statistics of Australia, New Zealand, Canada, Chile, and Iran, and the above mentioned eastern European countries are not included. The current study did observe a negative correlation between vaccination (X) and mortality or case-fatality ratio (Y) in a correlation method of X and Y/X.

Morbidity

When morbidity was analysed (Critical numbers/million population), the correlation was lesser (Figure 7, Panel A), with a variance of 15.7 percent benefit by influenza vaccination. Subsequent analysis after 1 week showed an increase in the equation's slope and intercept parameters (Figure 7, panel B) with a variance of 19.1 percent and the value is 7.3 percent on May18, 2020. There could be reasons for this observation. Mortality is a discrete and finite

variable, and the critical/serious position of the variable is a continuous variable subject to change with the progress of the disease, which could be improvement or death. Hence, a better parameter to assess morbidity would be the total number of critical cases so far/population, which is an ideal parameter required for the morbidity correlation. However, this parameter was not available for evaluation, which is a limitation of this study.

When the severe or critical case numbers were adjusted to the total number of cases per million population (case-morbidity ratio), the correlation was higher with R_2 of 0.41 (Figure 8 Panel A, worldometer data April 26, 2020), and value fluctuates around 0.34 ($r = -0.58$, Figure 8; May 7, 2020) and the latest value is 0.31 (May 18, 2020). This suggests a possibility for higher morbidity reduction. When the morbidity parameters were studied in a gap of 24 hours there were minimal changes in R_2 values (Figure 9, 2020) in morbidity parameters.

The primary parameter for morbidity is the need for ventilators, and this can reduce the ventilator requirement. The combined benefit for mortality and morbidity due to the influenza vaccine would be higher especially when the strategy for vaccination is used in adults >18 years instead of focusing on the elderly >65 years only.

Recovery

The recovery data was analysed, and it was adjusted to the cases per million. And further to the tests performed per million. The recovery data of the UK and Netherlands is not available in worldometer data to date (May 10, 2020), and some countries have not updated their recovery data. Also, recovery is a soft parameter that is subjected to over or under-reporting. With the available data and removal of 2 extreme variables in data (> 4 or 5 times of the maximum), the graph obtained shows a benefit for vaccination (R_2 0.06- after adjustment to tests, Figure 10 lower panel, May 10, 2020) and the was R_2 0.035 on May 18, 2020.

Proteomics

Transcriptomic analysis of host response showed an overlapping expression of differentially expressed genes (DEG's), genetic ontology (GO) terms, and protein-protein interaction (PPI) networks in response to Covid-19, SARS CoV, MERS CoV, Ebola, and H1N1 infections.³⁰ Gene network analysis, there was uniquely shared GO terms, or DEGs associated with host response of Covid-19 were H1N1-18, MERS CoV-38, SARS-CoV-20, and 28 for Ebola viruses. Among the unique shared genes in host response, the overlap between Covid-19 and

other infections were - H1N1 (43), MERS-CoV (112), SARS-CoV (30), and 116 for Ebola viruses.³⁰ PPI network and gene enrichment analysis showed an overlap of genes associated with MMP9, ICAM1, IL-6, CXCL1, TNF, CXCL8, TLR1, IRF 7, VEGF A, TLR2 which were expressed variably with significant overlap.³⁰ The T Cell and B cell response also has overlap between influenza A viruses and SARS-CoV-2.³¹ Among the five organisms, only H1N1 has an available vaccine, and rest other organism's vaccines are in the research and development stage. Hence, the H1N1 vaccine administration can prepare the host genes response to Covid-19 infections. Also, H1N1 vaccine-induced stem antibodies can inhibit the stem of haemagglutinin and the neuraminidase segment, which is an exhibition of pleiotropic effect of the vaccine.³²

Lower respiratory tract infections (LRI)

The incidence of influenza, viral, and bacterial lower respiratory tract infections (LRI) are much higher in South Asia and Southeast Asian countries than the western countries.¹⁶ Among the viral lower respiratory tract infections respiratory syncytial viruses and influenza virus infections are the commonest.^{16,33} South Asia and Southeast Asian countries have a high incidence of lower respiratory tract infections, 48.8 episodes/1000 population, and 45.9/1000 compared to high-income northern America (38.8/1000) and western Europe (28.7/1000). In the elderly population, the statistical numbers for LRI are 230/1000 and 181 /1000 when compared to high-income North America including Canada (73.2/1000) and western Europe (101/1000). Hence, in the elderly population, the dichotomy between these countries is more.

For comparison, the high-income Asian countries, including South Korea, Brunei, Singapore, and Japan, have LRI deaths (109 683/year) similar to high-income North America, including Canada (105 127 deaths/year) and comparable to Western Europe which comprises of 22 countries – 138 945 deaths/year. In the South Asia countries (India, Pakistan, Nepal, Bangladesh, Bhutan, and Afghanistan), it is 589 653 deaths/year, and in southeast Asia, it is 209 873 deaths/year.¹⁶ Moreover, these published results are well documented and organized data from reputed centres, predominantly from the urban and suburban population. In the rural community, the differences would be higher.

Influenza vaccination is very less in south Asian countries. Since influenza and LRI's are very common, and they will also have high herd immunity for influenza viruses, and hence the vaccination may not be required. Furthermore, overcrowding increases the spread of lower

respiratory tract infections, i.e., influenza or bacterial infections. Since diseases themselves are high, the need for vaccination is less. Also, the mortality of Covid-19 would increase in these countries in the next few months. However, the population-adjusted Covid-19 deaths would be significantly lower compared to western countries, which have higher mortality, due to the lower incidence of influenza, and respiratory tract infections.

South Korea, Australia, and New Zealand have emerged successfully so far with lesser mortality. Analysing the vaccination statistics of these countries is interesting. South Korea has a vaccination of 82 to 86%. New Zealand and Australia have a vaccination rate of about 65 and 73% respectively in age groups >65 years. The overall incidence of lower respiratory tract infections in high-income Asian countries is 45%, and in Australasia is 43.8%. Among the elderly, the LRI rates are 120.6 episodes/1000 and 165.6/1000 in high-income Asian countries and Australasia, respectively, compared to high income in North America and western Europe, which are 73.2/1000 and 101.3/1000.¹⁶ Hence, these countries (South Korea and Australasia) have higher LRI's and also higher vaccination rates, the combination of which could have helped to achieve the results. Moreover, these countries are known for their efficient testing and confinement methods, and the current results are of the early stages of the pandemic.

The central Latin American countries (including Mexico) document a lesser incidence of LRI deaths (43,191 deaths/year or 111/1000 people) and lower influenza vaccination rates. The pandemic started late in Mexico, and it is reporting more number of cases and mortality recently. Andean Latin American countries and Tropical Latin American countries like Brazil have higher LRI episodes and lower vaccination rates. There is a gradual fall in the incidence of H1N1 in Peru especially in Lima.³⁴ Also, they have higher mortality than Asian countries but less than western Europe and High-income North America.

In Andean Latin American countries (Peru, Bolivia, and Ecuador), even though the LRI episodes are higher, they have a vast land area, and overcrowding is significantly less; the herd immunity for influenza would be less. The population density of Peru is 26 Persons (P)/km², Brazil-25 P/km², whereas that of India is 464 P/km², Pakistan is 287 P/km², and the United States is 36 P/km². Hence central, Tropical, and Andean Latin American countries, based on this analysis, are also vulnerable though lesser than western Europe and High-income North America, and it is advisable to enhance vaccination with H1N1 with or without streptococcus pneumonia vaccine.

The mortality of Covid-19 is exponentially increases in the age group >50 years.^{35, 36} In the UK and US, the vaccination rates are 72% and 68%, respectively, in the age group of over 65 years. When the vaccination rates of age group > 50 years are combined, the overall vaccination rates would be about 50% only. Both these countries also have a sizable unregistered migrant population. When this data is connected, the vaccination will fall further mildly. Also, in the higher income western Europe and the US, the lower respiratory tract infections are lesser.

Among the small countries, Covid-19 death rates in Andorra (673/million population), Isle of Man (282/million), San Marino (1238/million), Channel Islands (276/million) and Bermuda (144/million) which are located in the western Europe and USA areas, is high. Sint Maarten – 350/million (Netherlands) and Montserrat- 200/million (UK) also has higher mortality. These small countries record a disproportionately higher mortality rate compared to other small countries with a comparable population.

Influenza attributable LRI

LRI's attributable to influenza was studied by the counterfactual method in the Global burden of disease study (GBD). From the published article, it could be observed that western Europe (137.5/100 000, CI 104-174) and high-income North America (281/100 000 population, CI 197-381) have a lower incidence of influenza attributable LRI's. Countries like Spain (91, CI 65-120), Italy (63, CI 44-85), France (134, CI 95-182) and UK (222, CI 158 to 257) have low influenza LRIs per 100 000 population. In the UK, Northern Ireland (139), Wales (132), and Scotland (163) have lower values compared to England (237) per 100 000.³⁷

Central Europe (358, 251-488), Eastern Europe (2399, CI 1717-3205), South Asia (1063, CI 725-1479), South East Asia (1591, CI 1118-2160), Central Asia (1292, CI 853-1652), North Africa and Middle East (775, CI 529-1077) have high influenza LRIs per 100 000 population.³⁷ High-income Asia Pacific has 146/100 000 (CI 102-197). High-income Asia Pacific group has less influenza incidence; the population density is very high - South Korea 510, Singapore 8000, Brunei 81, and Japan 347 P/Km², which could catalyse a herd immunity for influenza.

Central Latin American countries (443, CI 304 to 615) and Andean Latin American countries (695, CI 477 to 961) have higher rates of influenza attributable to lower respiratory tract infections per 100 000. However, Peru and Ecuador have lesser population density, as

discussed before. Taiwan (province of China) had high influenza rates of 976/100 000 (CI 681 to 1315) and has very little Covid-19 mortality (0.3/million population). Also, Taiwan recorded the highest influenza mortality -12.2/100 000 cases.³⁷ The influenza attributable LRIs in Vietnam was high – 3710/100 000 (CI 2537 to 5141), but so far, no Covid-19 mortality has been reported.

Adjacent countries like Brazil and Paraguay differ in mortality rates – Brazil (208/million) and Paraguay (2/million) population, and their influenza LRI incidence for Brazil is (268, CI 181 to 378) and Paraguay 738, CI 498-1034 per 100 000. Among the Scandinavian countries Norway 490, Finland-191, Denmark-137, Sweden-167 for 100 000 people were the influenza LRI rates³⁷, and their Covid-19 mortality rates are respectively Norway 45/million-population, Denmark 104/million, Finland 59/million, and Sweden 500/million. Countries like Poland (147, CI 101 to 200), Brunei (173, CI 118 to 241), Japan (141, CI 98 to 193), China (151, CI 104 to 208), Nicaragua (209, CI 139 to 296), and among the African countries - Mozambique (297, CI 201 to 419) and Ethiopia (329, CI 223 to 454)/100 000 have lower influenza LRI incidence per 100 000 population. Hence, these countries, as the pandemic evolves, may encounter higher Covid-19 severity.

Australia (125, CI 86 - 71) and New Zealand (193, CI 132-267) are associated with lesser influenza attributable LRIs per 100 000 population. Though these countries have initial success, there is a need for H1N1 vaccination in the adult and elderly population. North Africa (775, CI 529-1099) and Sub-Saharan countries (590, 408-510) have high influenza LRI's per 100 000, and these countries have higher population density also. Since the entire data is obtained from the contra factual strategy with a predictive regression model, the values of influenza attributable to LRI's may not be very accurate.

Figure 11 shows the incidence of influenza attributable LRI in population³⁷ and the Covid-19 mortality. In the table, for China, only Wuhan population was used. When the influenza incidence is less than 250 episodes/100 000, a significant rise in Covid-19 mortality is observed. Belgium, Andorra, UK, Spain, Italy, Sweden, China, France, USA, Netherlands, Ireland, Brazil, Canada, Switzerland, Luxembourg, Mexico, Portugal, Panama, Macedonia, Denmark, and Austria (Figure 11) were the countries in the descending levels of Covid-19 mortality.

In the influenza incidence segment of 500 to 1000/100 000, the Covid-19 mortality rate was less than 100/100 000 in most countries. Ecuador, Peru, and Chile were the exception, and they had mortality rates of about 230/million, and Bermuda and Iran showed mortality rates of 145 and 115/million, respectively. Ecuador, Peru, and Chile has a population density of about 25P/Km² each, and therefore, though they had higher influenza rates due to less population density, didn't catalyse to an active herd immunity of influenza. In the more upper segment of influenza incidence >1000/ 100 0000, only Armenia and Moldova were exceptions with mortality >100/million, and they have a population density of 103 and 123 P/Km² respectively.

The receiver operating characteristic curve (ROC) analysis (Figure 12) showed an increasing trend in the area under the curve (AUC), and for predicting the mortality >150/million, the AUC was 0.86. The AUC for predicting mortality >200/million is 0.85 for decreasing levels of influenza episodes. At the cut off value of 290 influenza LRI episodes/100 000, the sensitivity was 79 percent (CI 0.56 to 0.92), and the specificity was 88 percent (CI 0.82 to 0.92) to indicate Covid-19 mortality. Hence, the lower influenza LRI incidence is associated with higher Covid-19 mortality.

Germany had influenza attributable medically attended acute respiratory illness (iMAARI) in the 2018/2019 season of about 3 800 000 (CI 3.0 to 4.6 million), and physician certified influenza-associated incapacities of work were estimated to be 2.3 million (CI 2.1 to 2.5 million).³⁷ Also, a sizable number would have minimal symptoms or asymptomatic, and Germany has a population density of 240P/Km². Influenza attributed illness is much higher than the calculated GBD data, which determines as 101 000 LRI episodes in a year (2017).³⁸ The higher incidence of influenza could be the immunological mechanism of Germany's lesser mortality despite lesser influenza vaccination rates (37%) in the elderly (>65 years).

The influenza LRI incidence data and the lower respiratory tract infections' burden data is exhaustive and available for most countries.^{16,37} Hence, this data is more robust and thorough evidence for the concept than influenza vaccination data statistics. The population in Europe above 65 years is about 18 percent. Hence, the vaccination data in age >65 years may not represent the generalized population since Covid-19 mortality starts increasing after age 20.

Streptococcus Pneumonia vaccine

For further secondary prevention, streptococcus pneumonia vaccine would be a useful strategy which is known to be effective.^{39, 40} Bacterial infections are commonly associated with viral pneumonia.⁴¹ The strategical adjunct role of this streptococcus pneumonia vaccine has been discussed in the previous report.⁴² The addition of streptococcus pneumonia vaccine can further improve the protection benefits either by an additional or logarithmical value, which is yet to be determined.

In the current scenario, the spread of the coronavirus and problems are more in countries where the streptococcus pneumonia infection rates are low <100/DALYs/100000 (DALY-disability adjusted life years) with only very few countries in exception. The mortality of Covid-19 is higher in countries with lower respiratory tract infections - combined bacterial and viral infections are low (<200 DALYs/100000).³⁹ Countries like Italy, Spain and some neighboring countries recorded the lowest number of streptococcus pneumonia infections (<10 DALYs/100000).³⁹ South American, Africa, and many Asian countries have a rate of >1000/DALYs/100000. The current Covid-19 case fatality rate (June 26, 2020 worldometer) in Europe is 7.98%, North America 5.6%, Asia 2.5%, South America 3.92%, Africa is 2.6%, and in Oceania 1.36 percent.

Hence, in high-income countries or countries with a low incidence of LRI's or influenza attributable LRI's, it depends on influenza vaccination for immunity. Therefore, influenza vaccination is recommended in these countries - high income North America including Canada and Western Europe (including UK and Scandinavia) for the adult population, and enhancement of immunization in the elderly to reduce Covid-19 severity. The central Latin American, Andean Latin American countries also would benefit from H1N1 immunization. Australia and New Zealand, Brazil, China, Japan, Poland, and Brunei also would tend to benefit from this immunisation strategy. In low-income countries, high risk and high-income groups could be vaccinated to extrapolate the benefits of these observations since the mortality benefit for Covid-19 is a significant end-point. Therefore, even in low-income countries with a higher incidence of influenza, till a dedicated vaccination for Covid-19 is available H1N1 immunisation would a useful strategy.

With this analysis, there appears to be a direct link with influenza vaccination or the incidence of influenza LRIs in the general population with Covid-19 mortality. This is possibly by

modulating the immunity of the individuals, which could be innate or adaptive. Hence, there is a possibility for influenza (H1N1) vaccination for partial protection against coronaviruses especially in countries with a low incidence of lower respiratory tract infections or influenza LRIs. In appropriate circumstances streptococcus pneumonia vaccine can be also be supplemented.⁴² Recent study shows a significant declining trend in the antibody levels after primary infection. Hence, H1N1 vaccination would a useful measure to reduce mortality in Covid-19.⁴³

Cross-talk and Chaos

The immune system functions in many axes. Crosstalk between the neutrophils and lymphocytes,⁴⁴ as well as the microbiome and the immune system is a common phenomenon.⁴⁵ Also, stimulation of the immune system with these vaccines would efficiently build a defence, crosstalk, and 'chaos'⁴⁶ in the frontline, which would strengthen the immune system for SARS-Co-2 infections.

Future perspectives

CCR5-delta32 polymorphism and expression play an essential role as coreceptor in the virus entry stage of human immunodeficiency viruses⁴⁷ and also clearance of hepatitis C viruses.⁴⁸ Short genomic sequences similar to GP120 of human immunodeficiency virus have been noticed in SARS-Cov-2 spike proteins' genome.⁴⁹ CCR5 has a significant role in inflammatory pathogenesis in various systems.⁵⁰ It is well known that the SARS-CoV-2 virus entry is through ACE-2 receptors. The role of CCR5 is yet to be determined in SARS-CoV-2 infections. If there is an association between CCR5 and SARS-CoV-2 severity, CCR5 blockers like maraviroc can be studied for its plausible effects. Though CCR5 is a transmembrane protein coupled to G proteins⁵¹ and lacks ubiquitination,⁵² soluble CCR5⁵³ can be studied in plasma as a simpler technique instead of genetic polymorphism during the pandemic. The prevalence of Eurasian like reassortant G4 EA H1N1 swine influenza virus with 2009 pandemic virus genes has been observed recently,⁵⁴ which has potentials for human infection. Hence, in this scenario, also, H1N1 vaccines would be advantageous.

Streptococcus Pyogenes

Streptococcus pyogenes has immune regulatory potentials, and they are also potential candidates for vaccines and their effect is multifunctional.^{55, 56} It is worthwhile to investigate the role of these streptococcus pyogenes vaccines against SARS-CoV-2 viruses, which can

encompass a delicate balance of nature. The streptococcus pyogenes live vaccines can inhibit the viruses by endonucleases. It could help develop an immune response for host surveillance through M-protein type vaccines.⁵⁷

Conclusion

There is an association with Covid-19 severity and influenza vaccination status, which appears protective. Immunization with influenza vaccination and in appropriate circumstances with streptococcus pneumonia vaccine could be an effective strategy to reduce the severity of the Covid-19 disease in the general population.

Conflict of interests: None

Funding disclosure: None

Competing financial interests: None

Author statement: MCA conceived the idea, performed the analyses and wrote the paper. The views expressed in the paper are authors' own.

Table 1: Incidence of mortality and critical position of the patient and influenza vaccination status (age>65years) in different countries (April 10, 2020).

Country	Mortality/ Million population	Latest Influenza vaccination statistics (%)	Critical/Serious numbers (n)	Population in Million	Critical numbers/population in M
USA	50	67.5	10011	330	60.1
Spain	330	53.7	7371	47	59.7
Italy	302	52.7	3605	60	60.1
Germany	31	34.8	4895	82	59.7
France	187	49.7	7066	67	105.5
Iran	49	25	3987	66	60.4

UK	118	72.6	1559	81	19.2
Chile	3	64.7	360	18	20
Belgium	218	31	1285	11.5	111.7
Switzerland	110	38	386	8	48.2
Netherlands	140	64	1424	17.3	82.3
Canada	13	61.1	518	37.6	13.8
Austria	33	14	266	9	29.6
Portugal	40	60.8	241	10.3	23.3
South Korea	4	82.7	55	51.5	1.07
Sweden	79	49.4	719	10.2	70.4
Norway	20	34.4	82	5.4	15.1
Finland	8	48.4	78	5.5	14.1
Denmark	41	52	160	5.5	29.1
Luxembourg	83	37.6	30	0.6	50
Estonia	18	4.8	9	1.4	6.4
Iceland	18	45	11	0.37	29.7
Australia	2	73	81	24	3.3
New-Zealand	0.4	65	4	4.8	0.83
Ireland	53	57.6	165	4.9	33.7
Hungary	7	26.8	17	9.7	1.75
Israel	10	58.2	166	8.7	19.1
Lithuania	6	13.4	21	2.8	7.5
Czech Republic	10	20.3	96	10.5	9.1
Latvia	2	7.7	3	2	1.5
Serbia	8	11	112	7	16
Slovak republic	0.4	13	3	5.4	0.55
Turkey	11	7	1552	82	18.9
Slovenia	21	11.8	34	2.1	16.2

Table 2. Death/million population and tests performed/million population (Data April 14,2020).

Country	Latest Influenza vaccination statistics	Deaths in M/cases in M population	(Deaths/cases) *100/ Influenza vaccination	Tests/M
USA	67.5	4.0	5.9	8.8
Spain	53.7	10.5	19.5	12.8
Italy	52.7	12.8	24.3	17.3
Germany	34.8	2.4	7.0	15.7
France	49.7	10.9	22.0	5.1
Iran	25	6.3	25.1	3.4
UK	72.6	12.9	17.7	5.4
Chile	64.7	1.0	1.6	4.4
Belgium	31	13.4	43.1	8.8
Switzerland	38	4.5	11.7	22.3
Netherlands	64	10.8	16.8	6.7
Canada	61.1	3.1	5.1	11.5
Austria	14	2.7	19.5	16.8
Portugal	60.8	3.3	5.4	17.9
South Korea	82.7	1.9	2.3	10.2
Sweden	49.4	9.0	18.2	5.4
Norway	34.4	2.1	6.2	23.4
Finland	48.4	2.1	4.3	8.5
Denmark	52	4.6	8.9	12.7
Luxembourg	37.6	2.1	5.6	46.8
Estonia	4.8	2.2	46.3	24.3
Iceland	45	0.45	1.0	103.3
Australia	73	0.8	1.1	14.3
New-Zealand	65	0.7	1.1	13.5
Ireland	57.6	3.4	6.0	14.5
Hungary	26.8	8.3	30.9	3.7

Israel	58.2	1.0	1.8	13.5
Lithuania	13.4	2.3	17.1	15.6
Czech Republic	20.3	2.5	12.2	12.3
Latvia	7.7	0.9	11.2	15.3
Serbia	11	2.2	19.6	2.3
Slovak republic	13	0.26	2.0	5.5
Turkey	7	2.1	29.6	4.8
Slovenia	11.8	4.6	39.0	17.2

Figure 1. Correlation between influenza vaccination percentage, and (Cases per Million population)/vaccination percentage Panel A, May8, 2020, and Panel B May18, 2020. Panel C shows the case per-million value adjusted to tests performed (May 18, 2020) and Panel D and E data June 1 2020. Panel F shows linear and logarithmic trendlines (July 4 2020).

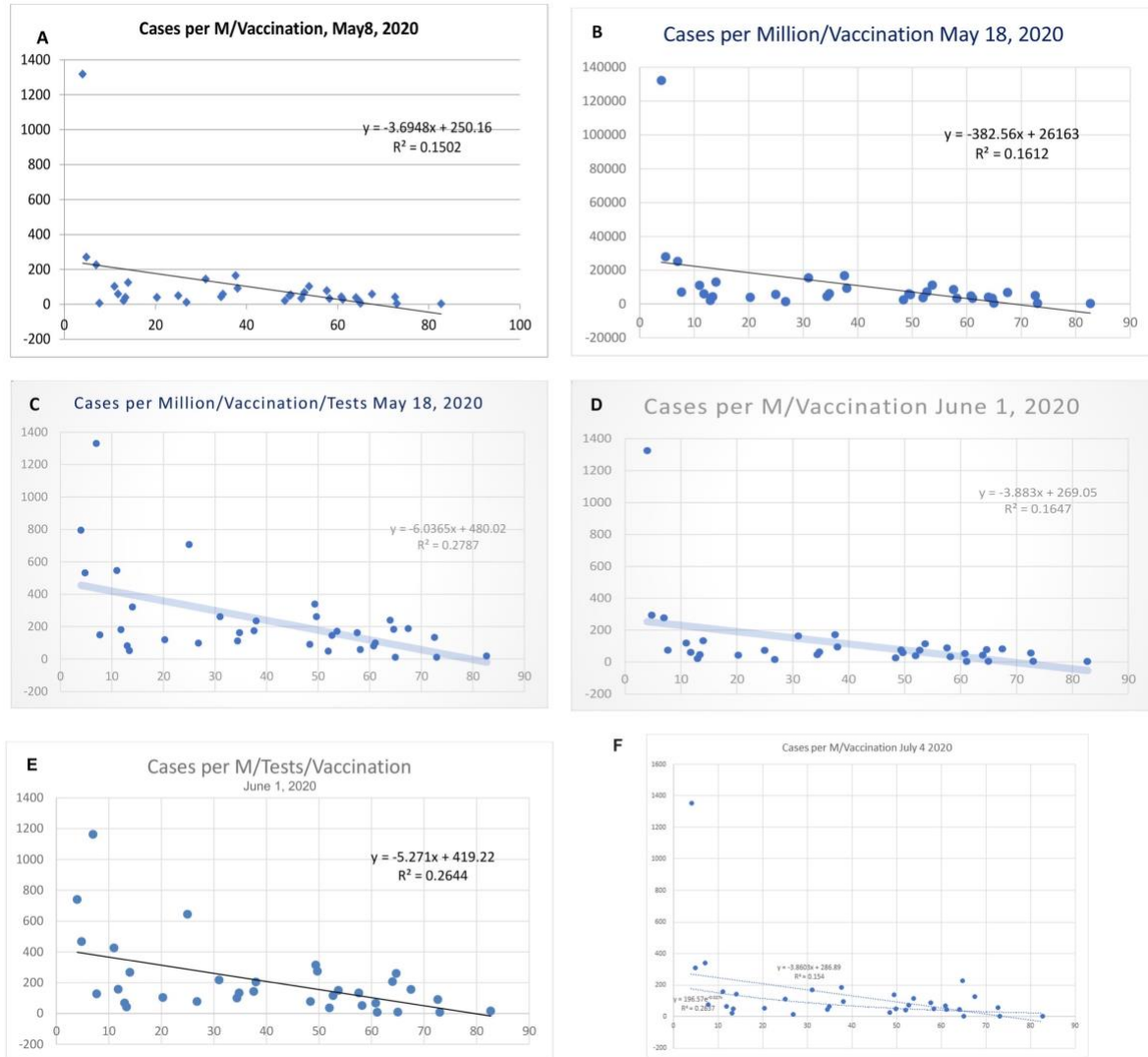


Figure 2. Correlation between influenza vaccination percentage (age>65yrs), and mortality per million population/vaccination percentage (Panel A-April 10,2020), Panel B April 15,2020, lower panel April 20, 2020, Panel C April 20,2020, Panel D April 25, 2020, Panel E May 1, 2020, Panel F May 8, 2020, Panel G May 31, 2020 and Panel H July 4, 2020).

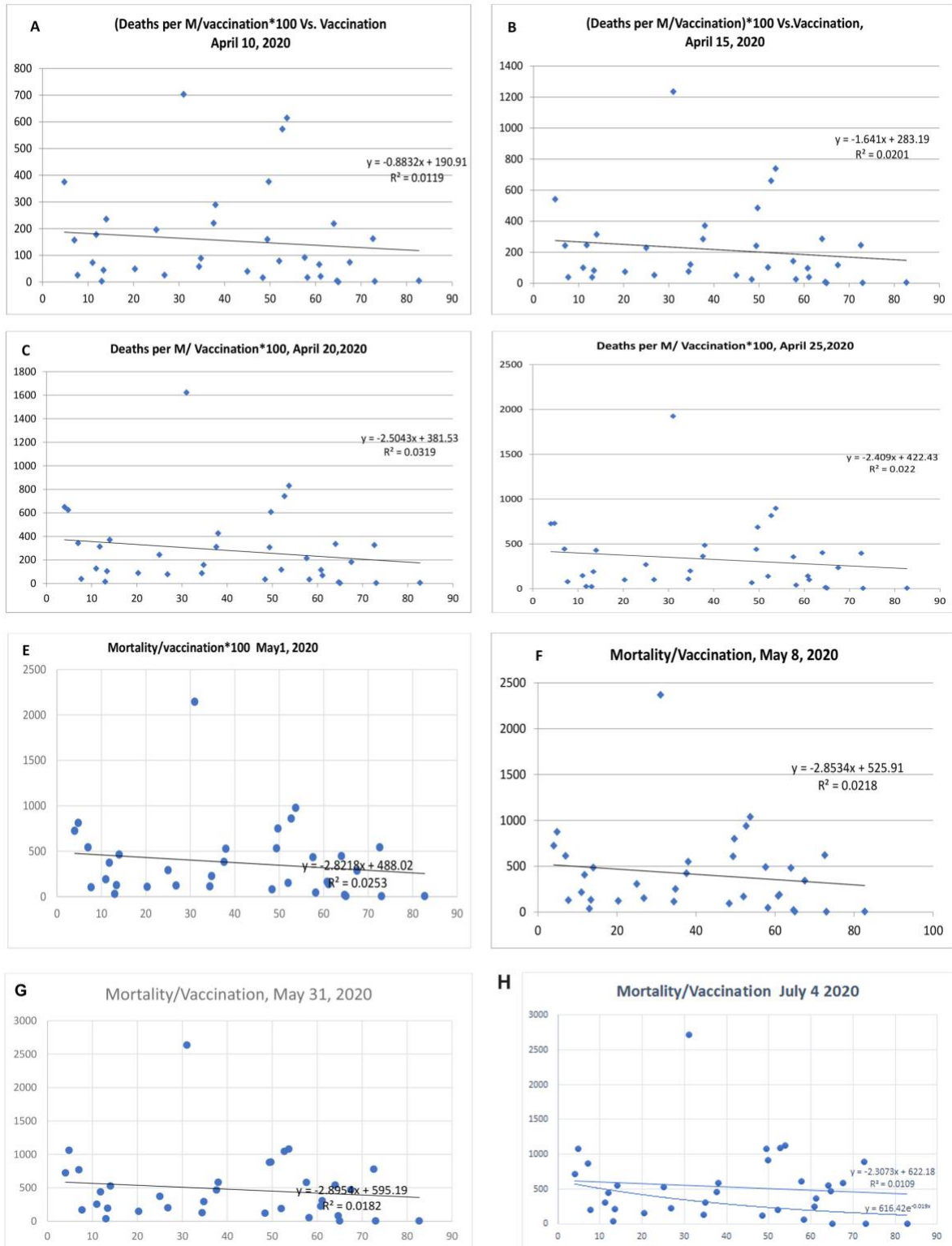
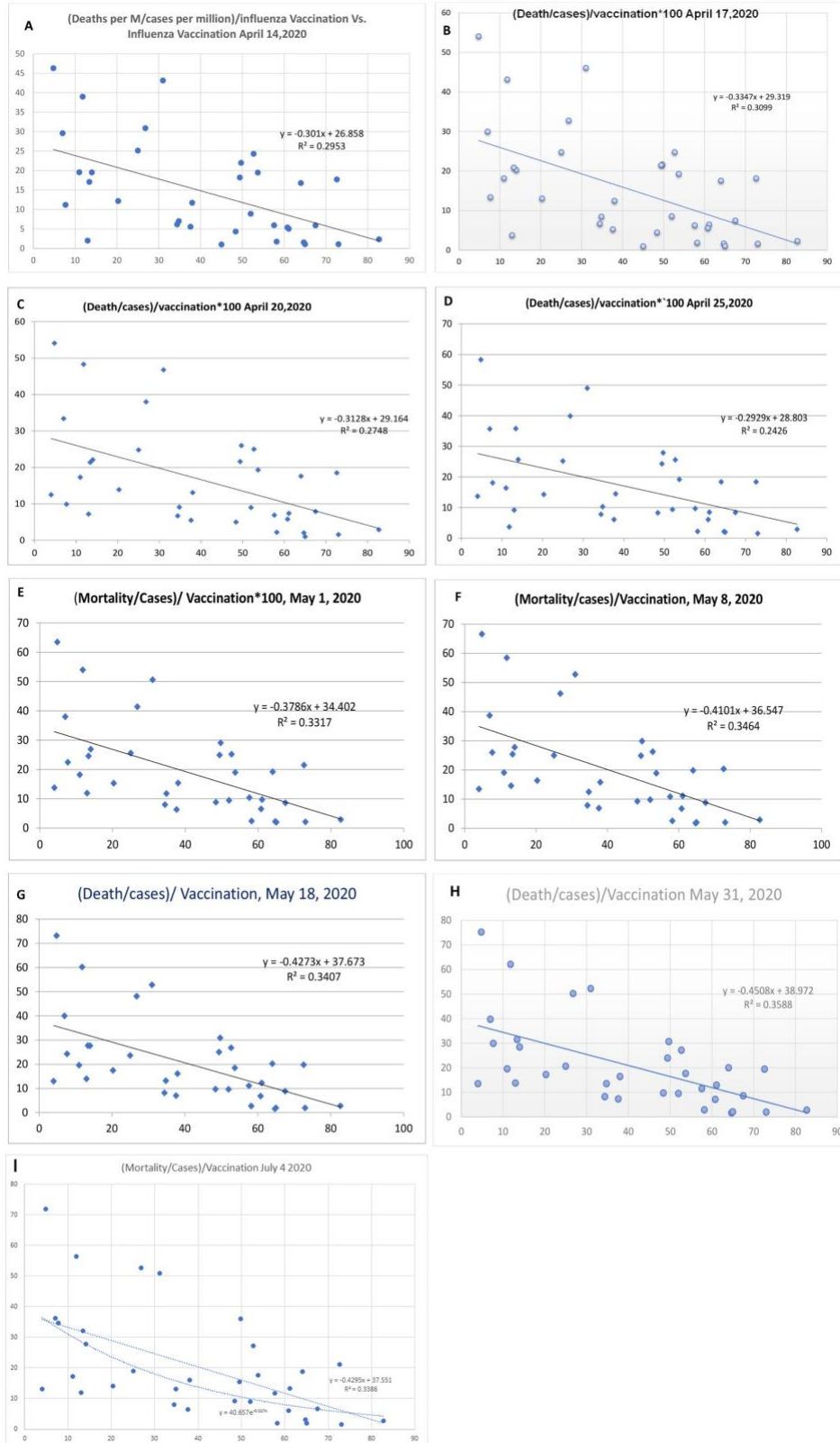


Figure 3. Correlation between influenza vaccination percentage Vs. [(Deaths/million)/Cases per million]/Vaccination (Panel-A April 14, 2020), Panel B April 17,2020), Panel C April 20, 2020, Panel D April 25, 2020, Panel E May 1, 2020, Panel F May8, 2020 and Panel G May 18, Panel H May 31, 2020 and Panel I July 4, 2020).



4. Correlation between vaccination and death per million/Cases per million adjusted to population (May 18, 2020) and tests performed (May 31, 2020).

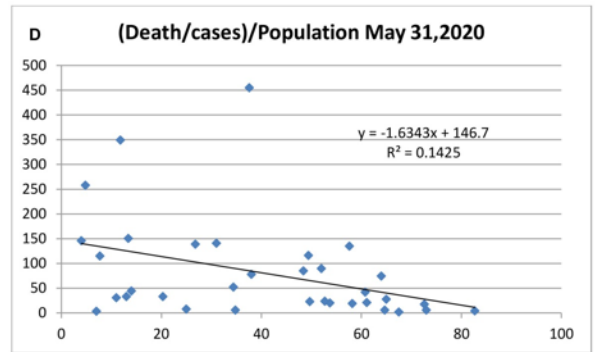
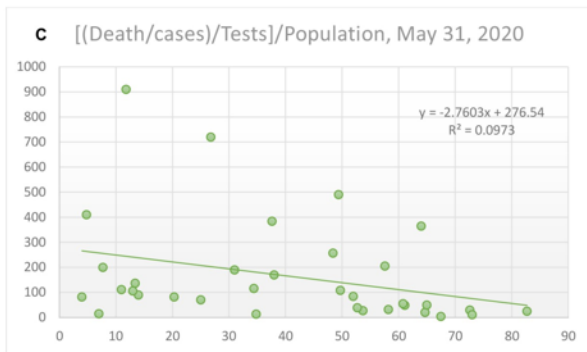
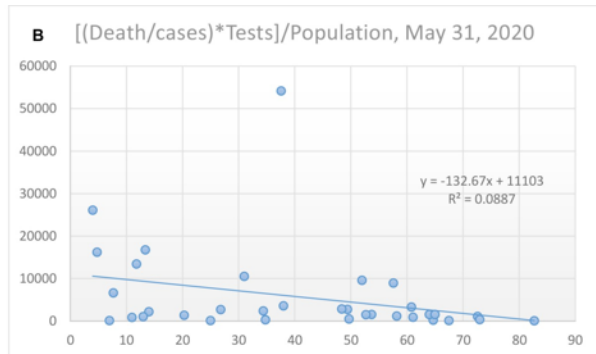
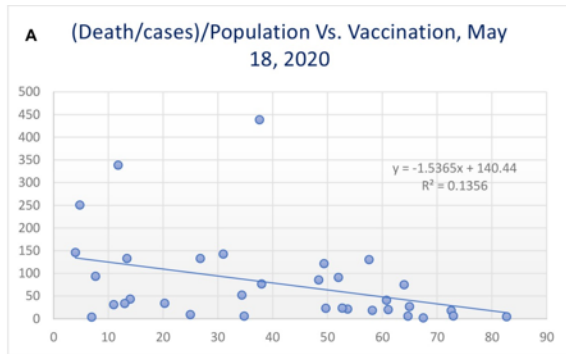
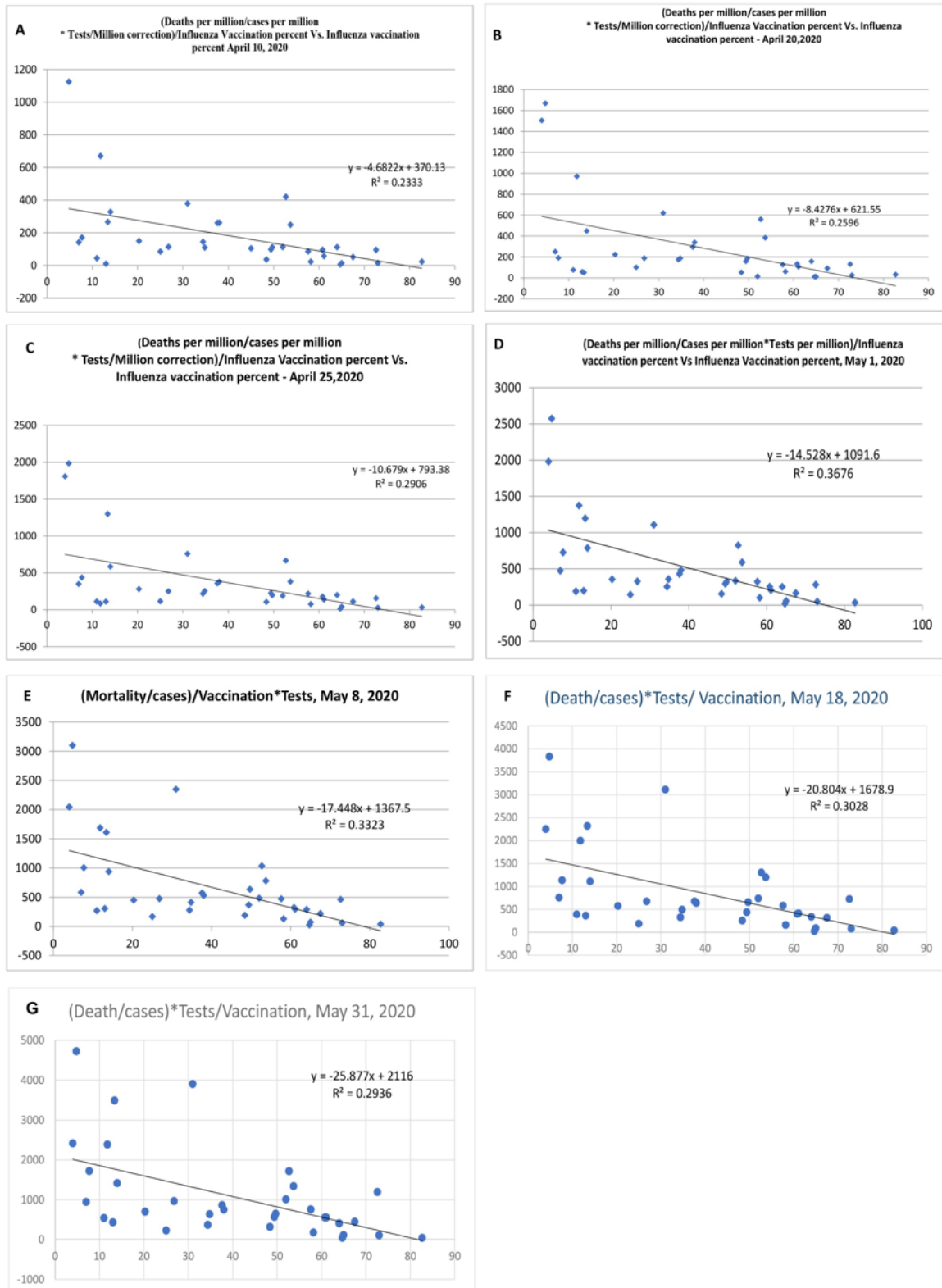


Figure 5. Correlation between influenza vaccination percentage Vs. [(Deaths/million)/Cases per million]/Vaccination after correction for tests performed per million. (Panel A April 10 2020, Panel B April 20 2020, Panel C April 25, 2020, Panel D May 1, 2020, Panel E May 8, 2020, Panel F May 18, 2020 and Panel G May 31,2020).



**Figure 6. Mortality/Cases adjusted to tests by denominator (Panel A, C and E).
Mortality/cases values adjusted to population in Panels B, D and F.**

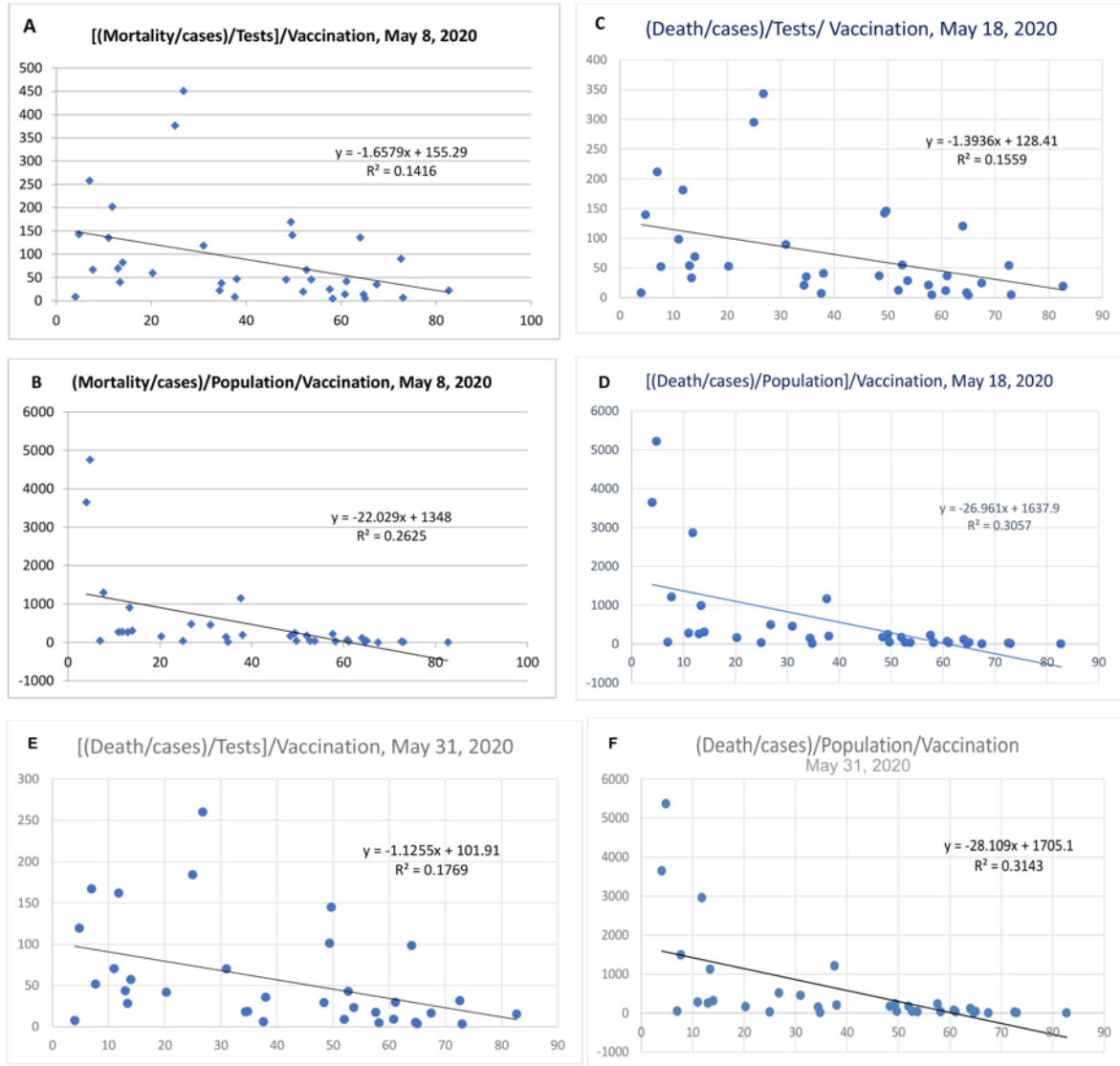


Figure 7. Correlation between influenza vaccination percentage, and [(critical number/million population)]/vaccination percentage (Panel A- April 10,2020, Panel B- April 18, 2020 and Panel C May 1, 2020, Panel D May 7 and Panel E May 18, 2020).

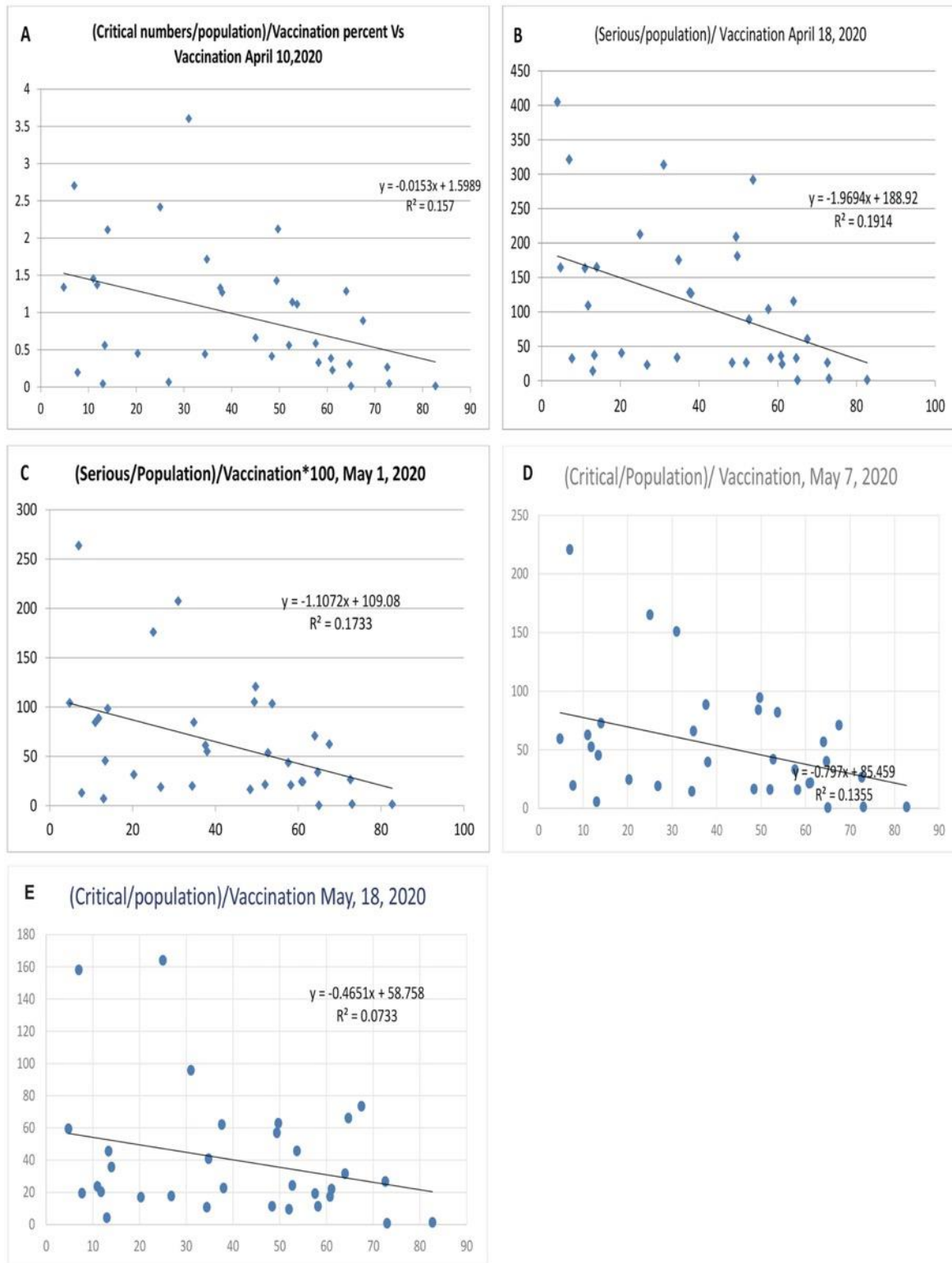


Figure 8. Correlation between influenza vaccination percentage, and [(critical number/million population)/ (total cases per million)]/vaccination percentage (Panel A April 26 2020, panel B May 1, 2020 and panel C May 8 2020, Panel D, May 18, 2020).

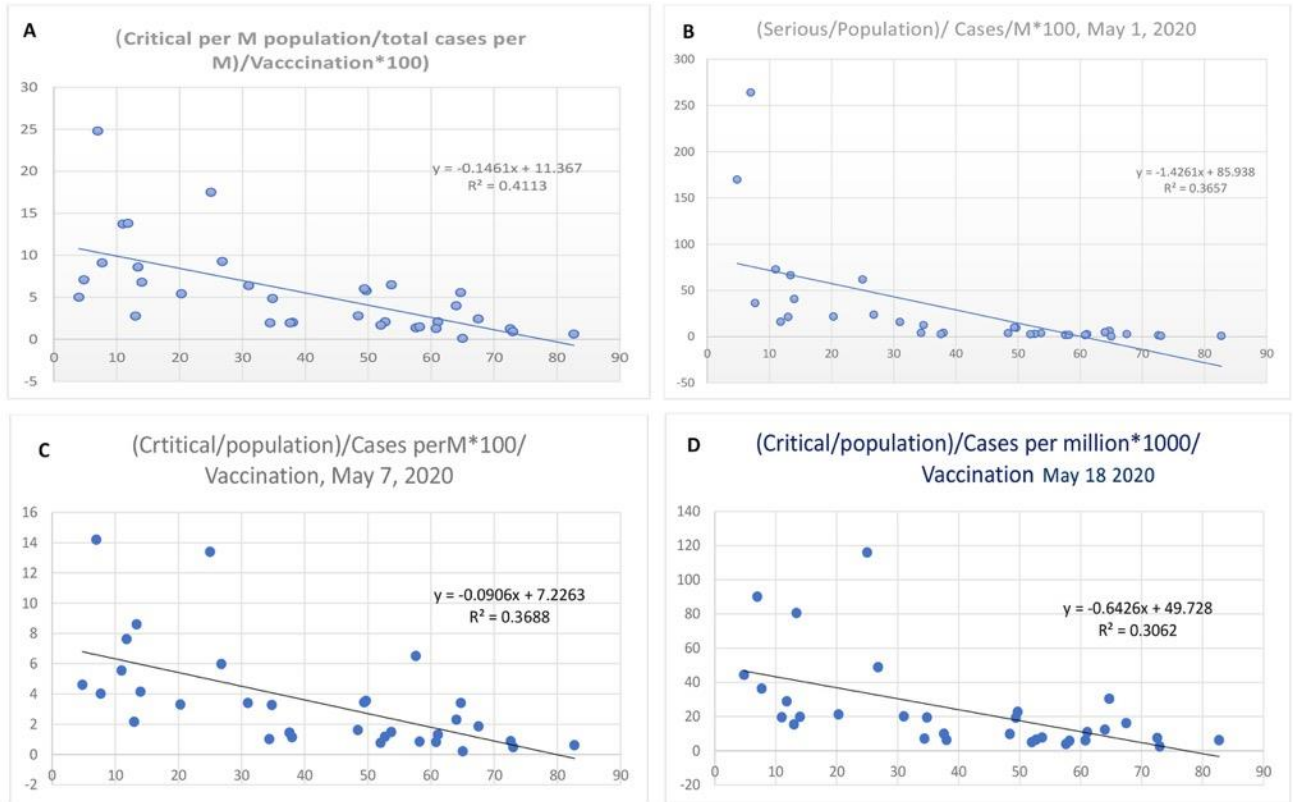


Figure 9. Correlation between influenza vaccination percentage and critical numbers evaluated in a 24hour period difference after May 7 on May 8, 2020.

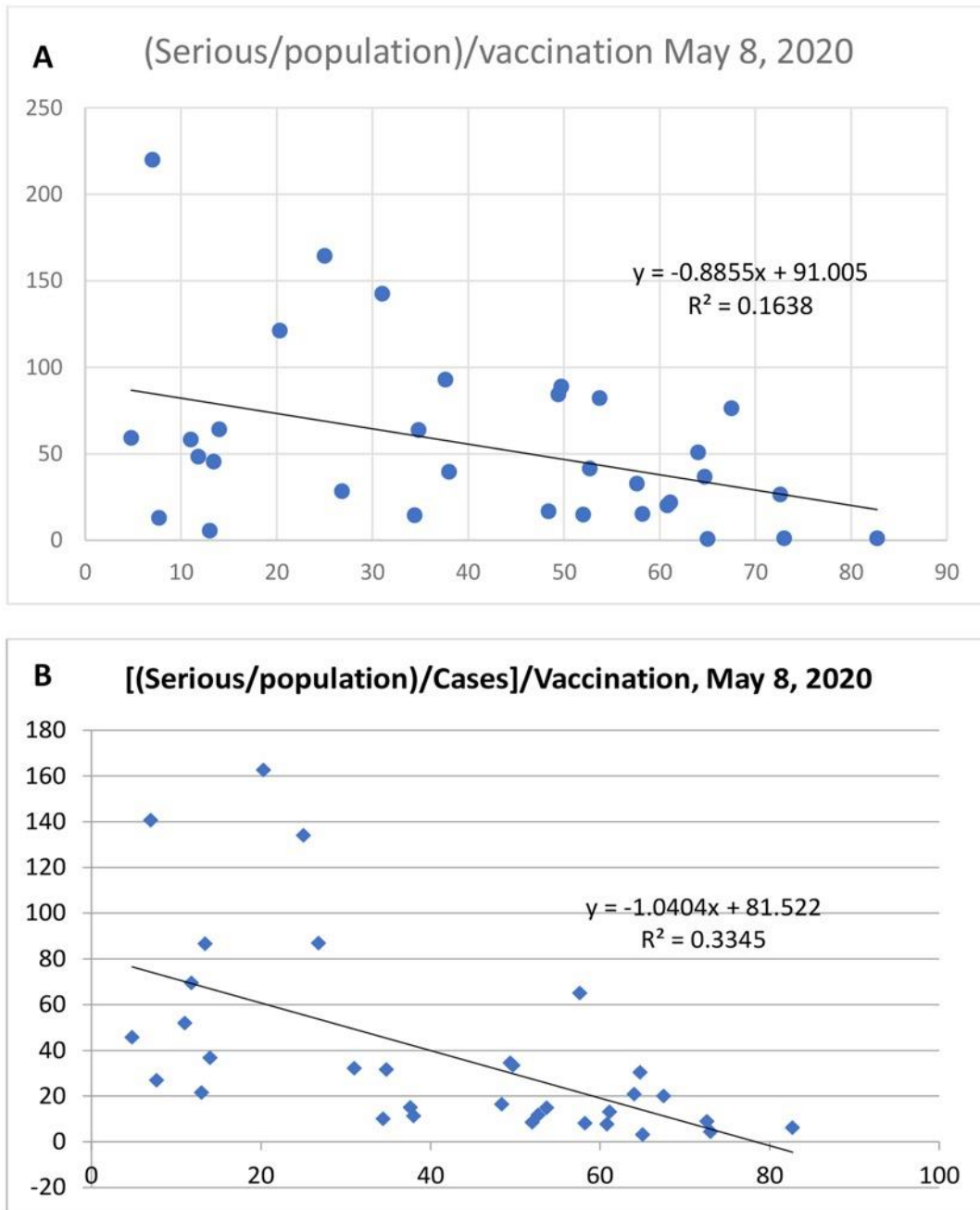
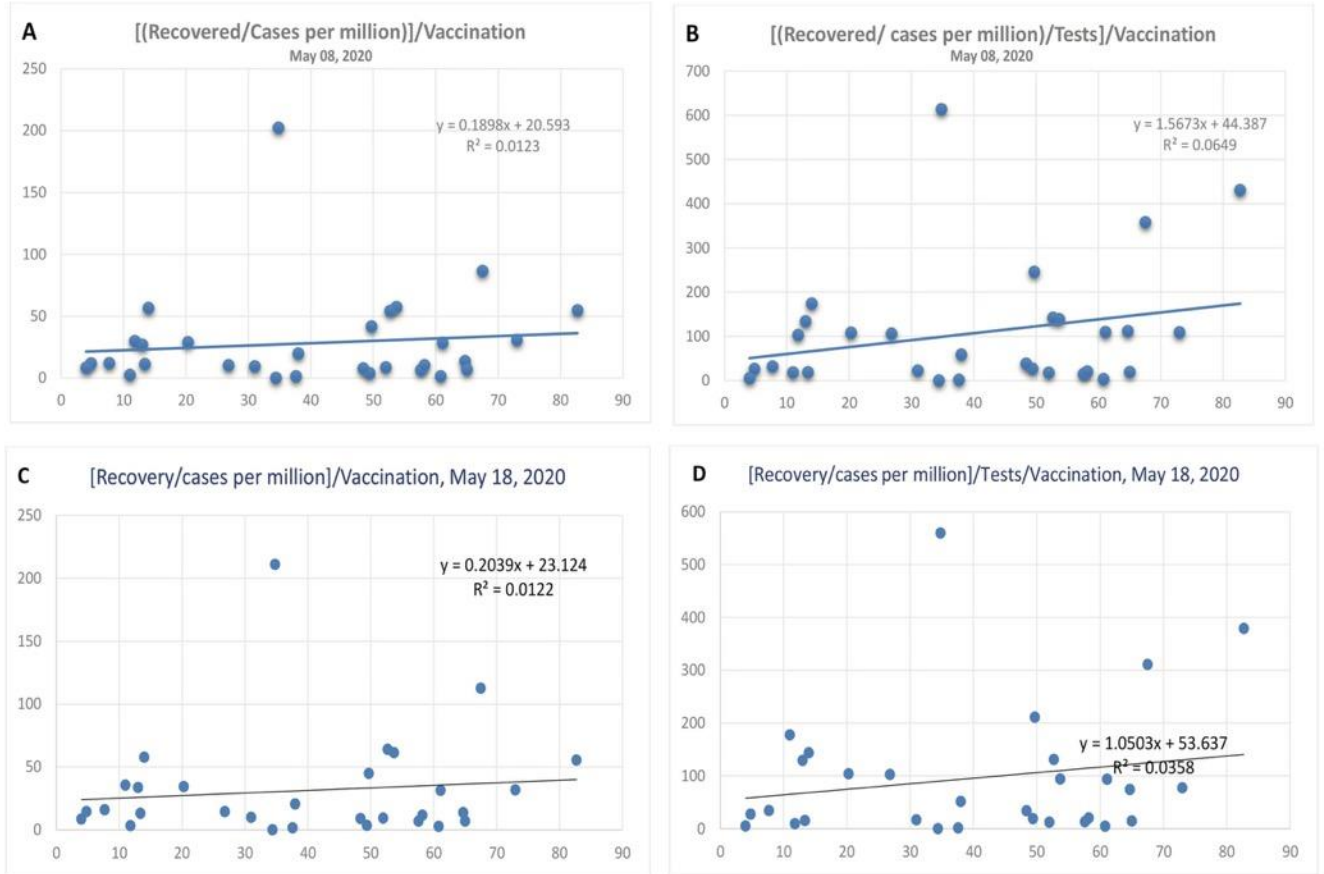


Figure 10. Correlation between influenza vaccination percentage and recovery parameters and adjusted to tests performed (Panels A and B, May 10, 2020; Panels C and D, May 18, 2020).



11. Figure shows the influenza incidence /100 000 population and Covid-19 mortality/million population (n=182).

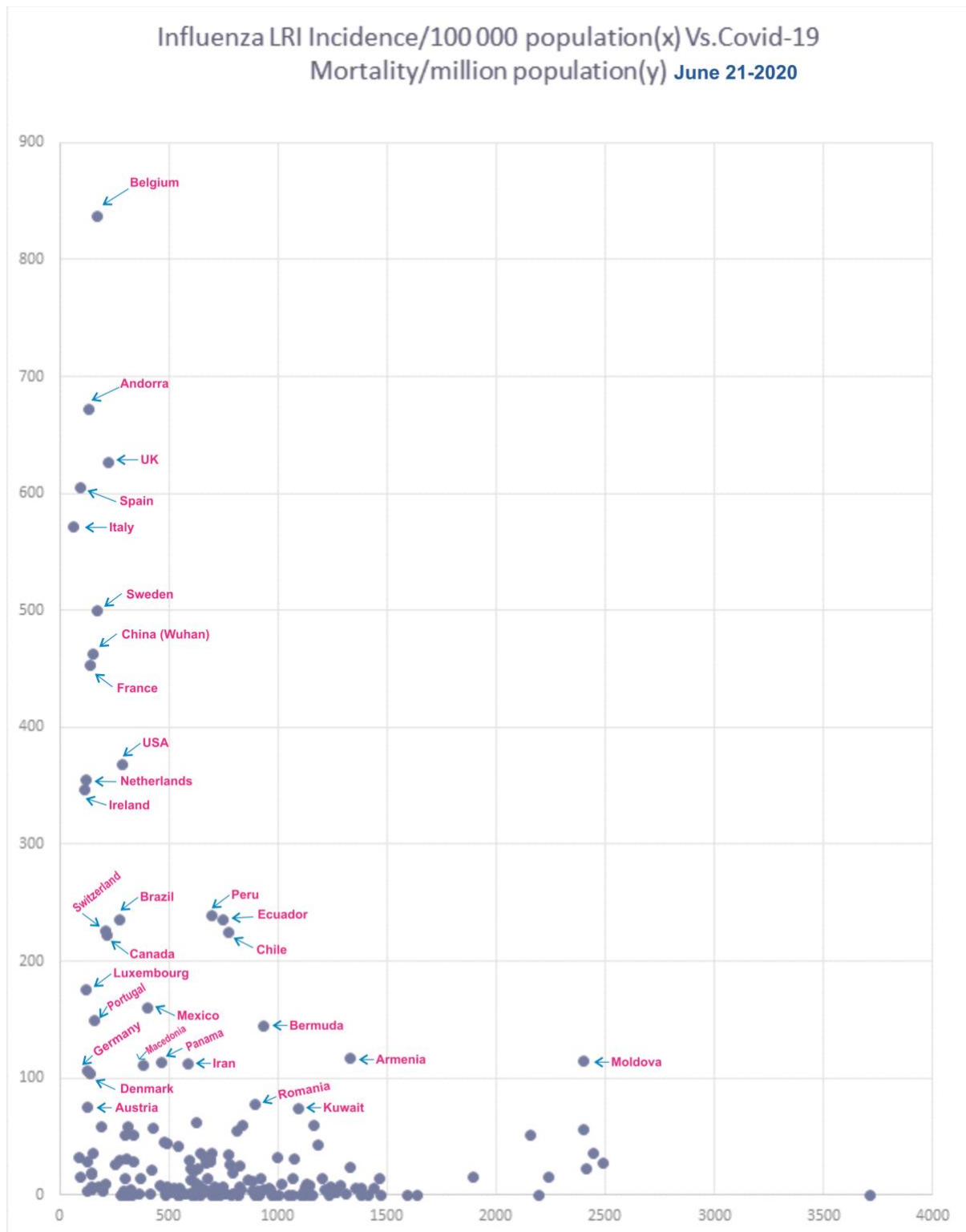
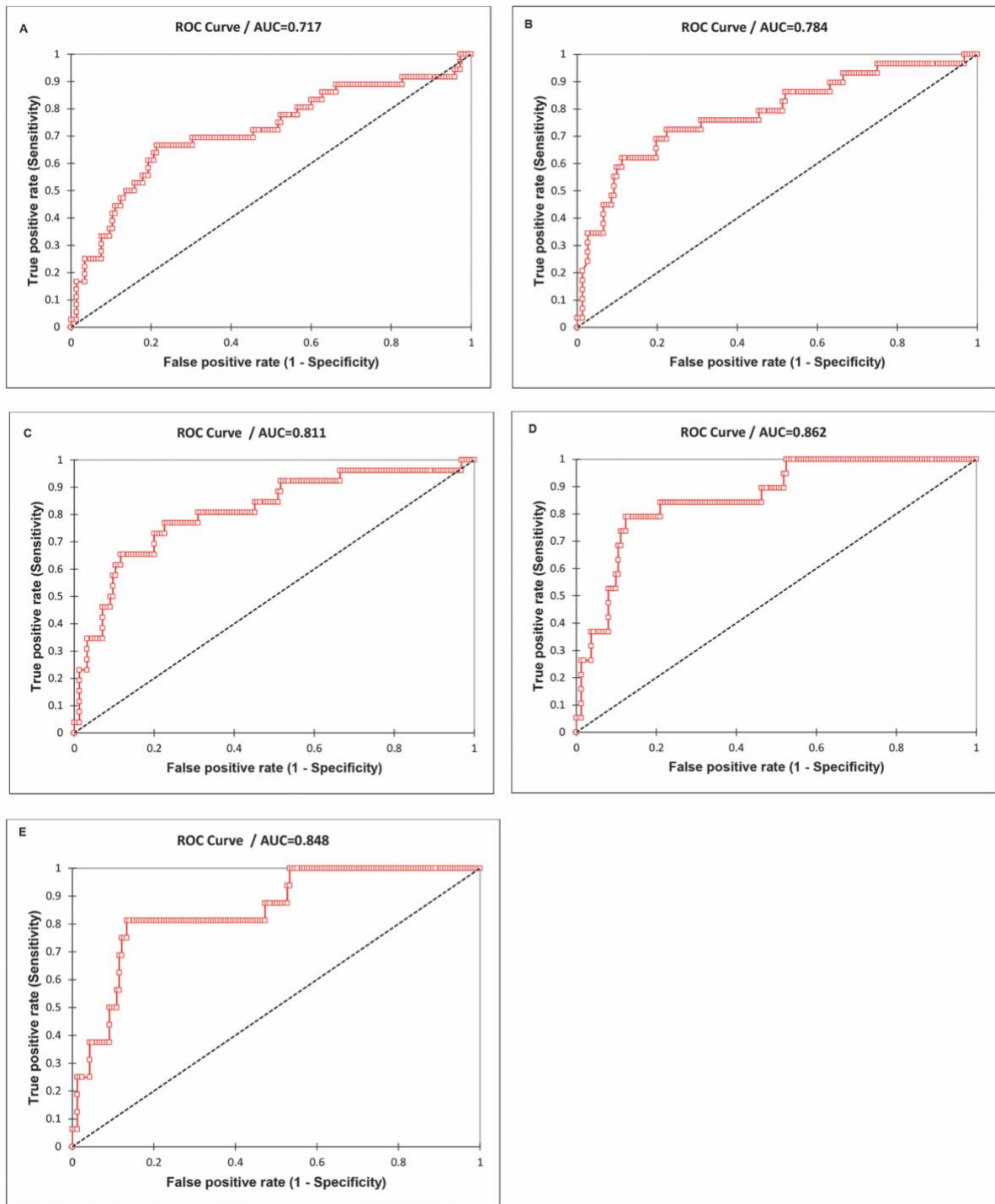


Figure 12. Receiver Operating Characteristics (ROC) curve analysis of the influenza incidence, and the mortality rates of Covid-19 (Cut off mortality rate at 50/million Area under the curve-AUC 0.72 Panel A, 75/million AUC 0.78 Panel B, 100/million AUC 0.81 Panel C, 150/million AUC 0.86 Panel D and 200/million AUC 0.85 Panel E – Data June 21, 2020).



Bibliography

1. Menachery V, Einfeld A, Schäfer A, Josset L, Sims A, Proll S et al. Pathogenic influenza viruses and coronaviruses utilize similar and contrasting approaches to control interferon-stimulated gene responses. *mBio*. 2014;5(3).
2. Zeng Q, Langereis M, van Vliet A, Huizinga E, de Groot R. Structure of coronavirus hemagglutinin-esterase offers insight into corona and influenza virus evolution. *Proceedings of the National Academy of Sciences*. 2008;105(26):9065-9069.
3. Li F. Structure, Function, and Evolution of Coronavirus Spike Proteins. *Annual Review of Virology*. 2016;3(1):237-261.
4. Yang P, Gu H, Zhao Z, et al. Angiotensin-converting enzyme 2 (ACE2) mediates influenza H7N9 virus-induced acute lung injury. *Sci Rep* 2014;4:7027-7027.
5. Dou D, Revol R, Östbye H, Wang H, Daniels R. Influenza A Virus Cell Entry, Replication, Virion Assembly and Movement. *Front Immunol*. 2018;9:1581. Published 2018 Jul 20. doi:10.3389/fimmu.2018.01581
6. Ramos I, Fernandez-Sesma A. Cell Receptors for Influenza a Viruses and the Innate Immune Response. *Frontiers in Microbiology*. 2012;3. <https://doi.org/10.3389/fmicb.2012.00117>
7. Liu X, Yang N, Tang J, et al. Downregulation of angiotensin-converting enzyme 2 by the neuraminidase protein of influenza A (H1N1) virus. *Virus Res*. 2014;185:64-71. doi:10.1016/j.virusres.2014.03.010.
8. Lisewski, AM. Association between Influenza Vaccination Rates and SARS-CoV-2 Outbreak Infection Rates in OECD Countries (March 20, 2020). Available at SSRN: <https://ssrn.com/abstract=3558270> or <http://dx.doi.org/10.2139/ssrn.3558270>.
9. OECD (2020), Influenza vaccination rates (indicator). doi: 10.1787/e452582e-en
<https://www.cdc.gov/flu/fluview/coverage-1819estimates.htm>.

10. Aliyari R , Imani S , Rezaei T , Shariati M , Hanifehzad Masooleh P , et al. Seasonal Influenza Vaccination Uptake and Its Socioeconomic Determinants in Patients and Staff of Hospitals in Shahroud, Northeast of Iran, Shiraz E-Med J. 2019 ; 20(4):e82898. doi: 10.5812/semj.82898.
11. <https://www.satista.com/statistics/1088880/share-of-people-vaccinated-against-influenza-in-belgium>.
12. Zürcher K, Zwahlen M, Berlin C, Egger M, Fenner L. Trends in influenza vaccination uptake in Switzerland: Swiss Health Survey 2007 and 2012. *Swiss Medical Weekly*. 2019;. doi.org/10.4414/smw.2019.14705.
13. Kunze U, Böhm G, Prager B, Groman E. Influenza vaccination in Austria: Persistent resistance and ignorance to influenza prevention and control. *Central European Journal of Public Health*. 2019;27(2):127-130. doi:10.21101/cejph.a5010.
14. https://www.ecdc.europa.eu/sites/default/files/documents/AER_for_2018_seasonal-influenza-corrected.pdf.
15. <https://apps.who.int/iris/bitstream/handle/10665/326242>.
16. Troeger C, Blacker B, Khalil I, Rao P, Cao J, Zimsen S et al. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet Infectious Diseases*. 2018;18(11):1191-1210. doi:[https://doi.org/10.1016/S1473-3099\(18\)30310-4](https://doi.org/10.1016/S1473-3099(18)30310-4)
17. Byeon KH, Kim J, Choi B, Choi BY. The coverage rates for influenza vaccination and related factors in Korean adults aged 50 and older with chronic disease: based on 2016 Community Health Survey data. *Epidemiol Health*. 2018;40:e2018034. doi:10.4178/epih.e2018034.
18. CDC.gov. Flu Vaccination Coverage, United States, 2018–19 Influenza Season.

19. Grabenstein J. Immunization to Protect the US Armed Forces: Heritage, Current Practice, and Prospects. *Epidemiologic Reviews*. 2006;28(1):3-26.
20. Straits-Tröster K, Kahwati L, Kinsinger L, Orelie J, Burdick M, Yevich S. Racial/Ethnic Differences in Influenza Vaccination in the Veterans Affairs Healthcare System. *American Journal of Preventive Medicine*. 2006;31(5):375-382.
21. Lone N, Simpson C, Kavanagh K, Robertson C, McMenamin J, Ritchie L et al. Seasonal Influenza Vaccine Effectiveness in the community (SIVE): protocol for a cohort study exploiting a unique national linked data set. 2020. <http://dx.doi.org/10.1136/bmjopen-2012-001019>.
22. Russell T, Hellewell J, Jarvis C, van Zandvoort K, Abbott S, Ratnayake R et al. Estimating the infection and case fatality ratio for coronavirus disease (COVID-19) using age-adjusted data from the outbreak on the Diamond Princess cruise ship, February 2020. *Eurosurveillance*. 2020;25(12).
23. Cruise ships, https://en.wikipedia.org/wiki/2020_coronavirus_pandemic_on_cruise_ships
https://en.wikipedia.org/wiki/2020_coronavirus_pandemic_on_cruise_ships
Ruby princess. 686 cases/18 mortality.
24. <https://www.cdc.gov/flu/professionals/healthcareworkers.htm>
25. <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html>
26. <https://www.livescience.com/covid-antibody-test-results-new-york-test.html>
27. <http://outbreaknewstoday.com/covid-19-antibody-study-in-sweden-75413/>
28. Carrasco-Hernandez R, Jácome R, López Vidal Y, Ponce de León S. Are RNA Viruses Candidate Agents for the Next Global Pandemic? A Review. *ILAR Journal*. 2017;58(3):343-358.

29. Consortium, EBMPHET, COVID-19 Severity in Europe and the USA: Could the Seasonal Influenza Vaccination Play a Role? (June 7, 2020). Available at SSRN: <https://ssrn.com/abstract=3621446> or <http://dx.doi.org/10.2139/ssrn.3621446>
30. Alsamman AM, Zayed H. The transcriptomic profiling of COVID-19 compared to SARS, MERS, Ebola, and H1N1. <https://doi.org/10.5281/zenodo.3783510>.
31. Blanco-Melo D, Nilsson-Payant B, Liu W, Uhl S, Hoagland D, Møller R et al. Imbalanced Host Response to SARS-CoV-2 Drives Development of COVID-19. *Cell*. 2020;181(5):1036-1045.e9.
32. Ivan Kosik, Davide Angeletti, James S. Gibbs, Matthew Angel, Kazuyo Takeda, Martina Kosikova, Vinod Nair, Heather D. Hickman, Hang Xie, Christopher B. Brooke, Jonathan W. Yewdell. Neuraminidase inhibition contributes to influenza A virus neutralization by anti-hemagglutinin stem antibodies. *The Journal of Experimental Medicine*, 2019; jem.20181624 DOI: 10.1084/jem.20181624.
33. Krishnan A, Kumar R, Broor S, et al. Epidemiology of viral acute lower respiratory infections in a community-based cohort of rural north Indian children. *J Glob Health*. 2019;9(1):010433. doi:10.7189/jogh.09.010433.
34. Tinoco YO, Azziz-Baumgartner E, Uyeki TM, et al. Burden of Influenza in 4 Ecologically Distinct Regions of Peru: Household Active Surveillance of a Community Cohort, 2009-2015. *Clin Infect Dis*. 2017;65(9):1532-1541. doi:10.1093/cid/cix565
35. Guilmoto C. COVID-19 death rates by age and sex and the resulting mortality vulnerability of countries and regions in the world. 2020; <https://doi.org/10.1101/2020.05.17.20097410>.
36. <https://www.worldometers.info/coronavirus/coronavirus-age-sex-demographics>.
37. Troeger C, Blacker B, Khalil I, Zimsen S, Albertson S, Abate D et al. Mortality, morbidity, and hospitalisations due to influenza lower respiratory tract infections, 2017: an analysis for the Global Burden of Disease Study 2017. *The Lancet Respiratory Medicine*. 2019;7(1):69-89.

38. https://www.rki.de/EN/Content/infections/epidemiology/inf_dis_Germany/influenza/summary_2018-19.htm
39. Brooks L, Mias G. Streptococcus pneumoniae's Virulence and Host Immunity: Aging, Diagnostics, and Prevention. *Frontiers in Immunology*. 2018;9.
40. Winje BA, Berild J, Vestheim et al. Efficacy and effectiveness of pneumococcal vaccination in elderly – an update of the literature. Norwegian Institute of Public Health. Dec 2019, www.fhi.no/en/publ/ ISBN digital: 978-82-8406-053-8.
41. Morris DE, Cleary DW, Clarke SC. Secondary Bacterial Infections Associated with Influenza Pandemics. *Front Microbiol*. 2017;8:1041. Published 2017 Jun 23. doi:10.3389/fmicb.2017.01041.
42. Arokiaraj, MC. Considering Interim Interventions to Control COVID-19 Associated Morbidity and Mortality – The Perspectives (March 27, 2020). Available at SSRN: <https://ssrn.com/abstract=3562102> or <http://dx.doi.org/10.2139/ssrn.3562102>.
43. Long Q, Tang X, Shi Q, Li Q, Deng H, Yuan J et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nature Medicine*. 2020; doi.org/10.1038/s41591-020-0965-6.
44. Costa S, Bevilacqua D, Cassatella M, Scapini P. Recent advances on the crosstalk between neutrophils and B or T lymphocytes. *Immunology*. 2018;156(1):23-32. 10.1111/imm.13005
45. Zeevi D, Korem T, Segal E. Talking about cross-talk: the immune system and the microbiome. *Genome Biol*. 2016;17:50. Published 2016 Mar 17. doi:10.1186/s13059-016-0921-4.
46. Mathias L. Heltberg, Sandeep Krishna, Mogens H. Jensen. On chaotic dynamics in transcription factors and the associated effects in differential gene regulation. *Nature Communications*, 2019; 10 (1) DOI: 10.1038/s41467-018-07932-1.

47. Van Der Ryst E. Maraviroc - A CCR5 Antagonist for the Treatment of HIV-1 Infection. *Frontiers in Immunology*. 2015;6.
48. Goulding C, McManus R, Murphy A, et al. The CCR5-delta32 mutation: impact on disease outcome in individuals with hepatitis C infection from a single source [published correction appears in *Gut*. 2005 Oct;54(10):1508. McManus, R [added]]. *Gut*. 2005;54(8):1157–1161. doi:10.1136/gut.2004.055699.
49. Pradhan P, Pandey A, Mishra A, Gupta P, Tripathi P, Menon M et al. Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag. 2020; doi.org/10.1101/2020.01.30.927871.
50. Vangelista L, Vento S. The Expanding Therapeutic Perspective of CCR5 Blockade. *Frontiers in Immunology*. 2018;8.
51. CCR5-Chemokine (C-C mitif) receptor 5 (gene/pseudogene). Genetics Home Reference.
52. Petti LM, Marlatt SA, Luo Y, Scheideman EH, Shelar A, DiMaio D. Regulation of C-C chemokine receptor 5 (CCR5) stability by Lys¹⁹⁷ and by transmembrane protein aptamers that target it for lysosomal degradation. *J Biol Chem*. 2018;293(23):8787-8801. doi:10.1074/jbc.RA117.001067.
53. Tsimanis A, Kalinkovich A, Bentwich Z. Soluble chemokine CCR5 receptor is present in human plasma. *Immunology Letters*. 2005;96(1):55-61.
54. Sun H, Xiao Y, Liu J, Wang D, Li F, Wang C et al. Prevalent Eurasian avian-like H1N1 swine influenza virus with 2009 pandemic viral genes facilitating human infection. *Proceedings of the National Academy of Sciences*. 2020;:201921186.
55. Arokiaraj MC, Wilson J. A Novel Method of Immunomodulation of Endothelial cells Using *Streptococcus Pyogenes* and its Lysate. *Biorxiv* 2020; doi:10.1101/2020.05.13.082180.
56. Dale JB, Batzloff MR, Cleary PP, et al. Current Approaches to Group A Streptococcal Vaccine Development. 2016 Feb 10. In: Ferretti JJ, Stevens DL, Fischetti VA, editors.

Streptococcus pyogenes : Basic Biology to Clinical Manifestations [Internet]. Oklahoma City (OK): University of Oklahoma Health Sciences Center; 2016. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK333413>

57. Vekemans J, Gouvea-Reis F, Kim J, Excler J, Smeesters P, O'Brien K et al. The Path to Group A Streptococcus Vaccines: World Health Organization Research and Development Technology Roadmap and Preferred Product Characteristics. *Clinical Infectious Diseases*. 2019;69(5):877-883.



SCHOOL OF LAW

UNIVERSITY of CALIFORNIA • IRVINE

Legal Studies Research Paper Series No. 2015-71

COMPULSORY VACCINATION LAWS ARE CONSTITUTIONAL

Erwin Chemerinsky

echemerinsky@law.uci.edu

University of California, Irvine ~ School of Law

Michele Goodwin

mgoodwin@law.uci.edu

University of California, Irvine ~ School of Law

The paper can be downloaded free of charge from SSRN at:

Essay

COMPULSORY VACCINATION LAWS ARE CONSTITUTIONAL

Erwin Chemerinsky & Michele Goodwin

ABSTRACT—A measles epidemic in California, that then spread to other states, focused national attention on the many children who have been vaccinated against communicable diseases. This Essay focuses on the constitutional issues concerning compulsory vaccination laws and argues that every state should require compulsory vaccination of all children, unless there is a medical reason why the child should not be vaccinated. There should be no exception to the compulsory vaccination requirement on account of the parents' religion or conscience, or for any reason other than medical necessity. The government's interest in protecting children and preventing the spread of communicable disease justifies mandatory vaccinations for all children in the United States.

AUTHORS—Erwin Chemerinsky is Dean and Distinguished Professor, and Raymond Pryke Professor of First Amendment Law, University of California, Irvine School of Law. Michele Goodwin is Chancellor's Professor of Law and Director, Center for Biotechnology and Global Health Policy, University of California, Irvine School of Law.

NORTHWESTERN UNIVERSITY LAW REVIEW

INTRODUCTION: THE CALIFORNIA EXPERIENCE.....	590
I. HISTORY OF COMPULSORY VACCINATION LAWS.....	595
II. COMPULSORY VACCINATION LAWS ARE ESSENTIAL.....	599
III. COMPULSORY VACCINATION LAWS ARE CONSTITUTIONAL.....	603
A. <i>Courts Have Consistently Rejected Constitutional Challenges to Compulsory Vaccination Laws</i>	604
B. <i>The Objection Based on Religious Freedom</i>	609
C. <i>Compulsory Vaccination Laws Meet Strict Scrutiny</i>	611
CONCLUSION	614

INTRODUCTION: THE CALIFORNIA EXPERIENCE

In December 2014, the first reported cases of measles arising in connection with Disneyland were reported. In the initial outbreak, forty-two people visiting or working at Disneyland were exposed to measles.¹ Measles is a highly communicable respiratory disease; the virus can linger on surfaces for up to two hours,² which can be disastrous for an amusement park, school, or even a neighborhood playground. The virus mostly spread among those who had not been vaccinated, either because they were too young or were not vaccinated by choice.³ By the end of January, the virus spread beyond the borders of California to infect children and even adults in Utah, Colorado, Washington, Oregon, and Mexico in a total of sixty-seven confirmed cases.⁴ Most of the January and December cases in California and beyond were linked to initial exposure at Disneyland.⁵ The outbreak ended in April 2015, when no new infections were reported after two incubation periods.⁶ Overall, approximately 147 people in the United

¹ Alicia Chang, *Disney Measles Outbreak that Sparked Vaccination Debate Ends*, KSL.COM (Apr. 17, 2015, 2:51 PM), <http://www.ksl.com/?nid=157&sid=34278095> [<http://perma.cc/M9LH-UZHT>].

² Lisa Aliferis, *Disneyland Measles Outbreak Hits 59 Cases and Counting*, NPR (Jan. 22, 2015, 12:24 PM), <http://www.npr.org/sections/health-shots/2015/01/22/379072061/disneyland-measles-outbreak-hits-59-cases-and-counting> [<http://perma.cc/JT3X-KEWY>].

³ Ralph Ellis et al., *Outbreak of 51 Measles Cases Linked to Disneyland*, CNN (Jan. 23, 2015, 3:04 PM), <http://www.cnn.com/2015/01/21/health/disneyland-measles/index.html> [<http://perma.cc/ML3B-ZC4G>].

⁴ Adam Nagourney & Abby Goodnough, *Measles Cases Linked to Disneyland Rise, and Debate Over Vaccinations Intensifies*, N.Y. TIMES (Jan. 21, 2015), <http://www.nytimes.com/2015/01/22/us/measles-cases-linked-to-disneyland-rise-and-debate-over-vaccinations-intensifies.html> [<http://perma.cc/T3AH-NZKW>].

⁵ Jonathan Corum et al., *Facts About the Measles Outbreak*, N.Y. TIMES (Feb. 6, 2015), http://www.nytimes.com/interactive/2015/02/02/us/measles-facts.html?_r=0 [<http://perma.cc/9SW8-QRRX>].

⁶ Chang, *supra* note 1.

States were infected.⁷ This outbreak was the worst in California in twenty-four years, but luckily there were no reported deaths.⁸

According to the California Department of Public Health, measles, mumps, and rubella (MMR) vaccinations “are more than 97% effective in preventing measles.”⁹ However, in the past few years, more and more parents have declined to vaccinate their children. In California, from 2007 to 2013 the rate of kindergarten parents refusing to vaccinate their children under a personal belief exemption doubled.¹⁰ One reason for this precipitous drop in vaccinations in the last few years is largely due to the medically unsupported theory that inoculation could lead to autism among children. Parents and even some scholars¹¹ point to a 1998 article published in *The Lancet* written by Dr. Andrew Wakefield and his colleagues.¹² The article inferred a cause and effect between autism and the MMR vaccine. The impact of his article was swift and profound. According to one article, “tens of thousands of parents around the world” were turned against the MMR vaccine.¹³

Yet, the study had many flaws. Dr. Wakefield’s study consisted only of twelve children who were selectively screened and chosen to participate. Moreover, the study was partially funded by attorneys hired by parents to sue vaccine manufacturers. Nevertheless, Dr. Wakefield’s research was quoted by newspapers throughout the world, raising alarm about the

⁷ *Id.*

⁸ *See id.*; Phil Willon & Melanie Mason, *California Gov. Jerry Brown Signs New Vaccination Law, One of Nation’s Toughest*, L.A. TIMES (June 30, 2015, 9:11 PM), <http://www.latimes.com/local/political/la-me-ln-governor-signs-tough-new-vaccination-law-20150630-story.html#page=1> [<http://perma.cc/U58T-SKZQ>].

⁹ Press Release, Cal. Dep’t of Pub. Health, *Measles Outbreak that Began in December Now Over* (Apr. 17, 2015), <https://www.cdph.ca.gov/Pages/NR15-029.aspx> [<https://perma.cc/UPD2-G53C>].

¹⁰ Aliferis, *supra* note 2.

¹¹ MARK NAVIN, VALUES AND VACCINE REFUSAL: HARD QUESTIONS IN ETHICS, EPISTEMOLOGY, AND HEALTHCARE 42 (2016) (stating that “[m]any vaccine denialists have rallied around Wakefield”); Fiona Godlee et al., *Wakefield’s Article Linking MMR Vaccine and Autism was Fraudulent: Clear Evidence of Falsification of Data Should Now Close the Door on this Damaging Vaccine Scare*, 342 *BMJ* 64 (2011); Laura Eggertson, *Lancet Retracts 12-Year-Old Article Linking Autism to MMR Vaccines*, 182 *CANADIAN MED. ASS’N J.* E199, E199 (2010) (stating that parents “seized upon the apparent link” between vaccines and autism); Philip J. Smith et al., *Parental Delay or Refusal of Vaccine Doses. Childhood Vaccination Coverage at 24 Months of Age, and the Health Belief Model*, 126 *PUB. HEALTH REP. (SUPPLEMENT 2: ASSESSMENT OF VACCINATION COVERAGE)* 135, 144 & tbl.5 (2011) (explaining that many parents who delay or refuse to vaccinate their children cite autism as a main reason).

¹² A.J. Wakefield et al., *Ileal-Lymphoid-Nodular Hyperplasia, Non-Specific Colitis, and Pervasive Developmental Disorder in Children*, 351 *LANCET* 637 (1998). The article was retracted in February 2010. Editors of the *Lancet*, *Retraction—Ileal-Lymphoid-Nodular Hyperplasia, Non-Specific Colitis, and Pervasive Developmental Disorder in Children*, 375 *LANCET* 445 (2010).

¹³ Eggertson, *supra* note 11, at E199; *see also* Smith et al., *supra* note 11.

efficacy and safety of vaccines.¹⁴ Even politicians “sow[ed] suspicion” about the safety of vaccination and urged parents to be cautious.¹⁵ Eventually, *The Lancet* retracted Wakefield’s study, criticizing fundamental aspects of the paper as “incorrect.”¹⁶ As well, subsequent research disproved Wakefield’s findings, including a recent study involving over 95,000 children with older autistic siblings, found that the relative risk of autism among vaccinated children with older autistic siblings was lower compared to unvaccinated children.¹⁷

Parents opposed to vaccinations (often referred to as anti-vaxxers) claim the dramatic rise in autism cases in the United States prove that vaccines are harmful and vindicate Wakefield’s early findings. In an effort to “protect” their children from vaccination, anti-vaxxers have used various legislative “opt-outs” or exemptions to spare their children from vaccination. As of June 2015, more than 80,000 California students claim personal belief exemptions annually.¹⁸

Despite the rising fears of vaccination, the benefits of measles vaccines are well documented. Within the first twenty years of licensed measles vaccination in the United States, an estimated fifty-two million cases and fifty-two hundred deaths were prevented.¹⁹ Additionally, due to the effectiveness of that vaccine, the United States declared measles to be eliminated from the country in 2000.²⁰ That was a significant victory for modern medicine. So what accounted for the most recent outbreak?

¹⁴ See, e.g., Philip J. Hilts, *House Panel Asks for Study of a Vaccine*, N.Y. TIMES (Apr. 7, 2000), <http://www.nytimes.com/2000/04/07/us/house-panel-asks-for-study-of-a-vaccine.html> [<http://perma.cc/92LR-AKR9>]; see also Michael J. Smith et al., *Media Coverage of the Measles-Mumps-Rubella Vaccine and Autism Controversy and Its Relationship to MMR Immunization Rates in the United States*, 121 PEDIATRICS 836, 839 fig.1 (2008). For a summary of MMR vaccine coverage in British media markets, see Tammy Speers & Justin Lewis, *Journalists and Jabs: Media Coverage of the MMR Vaccine*, 1 COMM. & MED. 171, 173 tbl.1 (2004).

¹⁵ Scott Gottlieb, *Why Debate Over Vaccines and Autism Will Continue*, FORBES (Feb. 4, 2015, 4:34 AM), <http://www.forbes.com/sites/scottgottlieb/2015/02/04/why-debate-over-vaccines-and-autism-will-continue/> [<http://perma.cc/77MB-Y7RR>]; Carrie Dann, *Rand Paul: Vaccines Can Lead to ‘Mental Disorders’*, NBC NEWS (Feb. 2, 2015, 5:07 PM), <http://www.nbcnews.com/politics/elections/rand-paul-vaccines-can-lead-mental-disorders-n298821> [<http://perma.cc/X2RW-28LR>] (quoting Rand Paul as saying, “I have heard of many tragic cases of walking, talking normal children who wound up with profound mental disorders after vaccines”).

¹⁶ Editors of the *Lancet*, *supra* note 12, at 445.

¹⁷ Anjali Jain et al., *Autism Occurrence by MMR Vaccine Status Among US Children With Older Siblings With and Without Autism*, 313 JAMA 1534, 1536 (2015).

¹⁸ Willon & Mason, *supra* note 8.

¹⁹ Alan B. Bloch et al., *Health Impact of Measles Vaccination in the United States*, 76 PEDIATRICS 524, 530 (1985).

²⁰ See Corum, *supra* note 5.

Measles outbreaks in the United States, such as the one in Disneyland, have largely been attributed to those carrying the disease from other countries into the United States.²¹ Travelers abroad can become infected—especially in countries that lack “herd immunity”²² or high vaccination rates of the United States—and then spread the disease among the unvaccinated back home. Therefore, although the United States’ high vaccination rates and herd immunity serve as a global model, vaccines continue to be important because outbreaks still can (and do) occur among those not immunized as demonstrated in the Disneyland case.

As a result of the California outbreak, pressure was exerted on the legislature to change state law.²³ At the end of June 2015, Governor Brown signed into law SB 277.²⁴ This bill eliminated personal and religious belief vaccination exemptions for children enrolled in school or daycare. Under SB 277, a parent can continue to decline vaccinations for his or her child for religious or personal reasons, but only if the child is enrolled in a home-based private school or off-campus independent study program.²⁵ Moreover, unvaccinated children can utilize their exemptions obtained before 2016 until they enter either kindergarten or the seventh grade, depending on their age.²⁶ Additionally, parents may still obtain medical exemptions for their children and the law permits doctors to take family history or sibling health into account in deciding whether to issue a medical exemption.²⁷

The bill goes into effect on July 1, 2016, and will make California the third state in the nation to require compulsory vaccination law with no religious or personal belief exemptions.²⁸ In a prepared statement, Governor

²¹ See Mark Berman, *How the U.S. Went from Eliminating Measles to a Measles Outbreak at Disneyland*, WASH. POST: POST NATION (Jan. 23, 2015), <http://www.washingtonpost.com/news/post-nation/wp/2015/01/23/how-the-u-s-went-from-eliminating-measles-to-a-measles-outbreak-at-disneyland> [https://perma.cc/LS39-DNAR].

²² Emily Willingham & Laura Helft, *What is Herd Immunity?*, PBS (Sep. 9, 2014), <http://www.pbs.org/wgbh/nova/body/herd-immunity.html> [http://perma.cc/G447-MKPW] (“The term ‘herd immunity’ refers to a means of protecting a whole community from disease by immunizing a critical mass of its populace. Vaccination protects more than just the vaccinated person. By breaking the chain of an infection’s transmission, vaccination can also protect people who haven’t been immunized. But to work, this protection requires that a certain percentage of people in a community be vaccinated.”).

²³ See Willon & Mason, *supra* note 8.

²⁴ S.B. 277, 2015–16 Leg., Reg. Sess. (Cal. 2015) (approved by Governor Jerry Brown on June 30, 2015).

²⁵ *Id.* § 2.

²⁶ *Id.*

²⁷ *Id.* § 5.

²⁸ The other two states are Mississippi and West Virginia. Sarah Kaplan, *The California Assembly Just Approved One of Nation’s Strictest Mandatory Vaccine Laws*, WASH. POST (June 26, 2015),

Brown remarked that “[t]he science is clear that vaccines dramatically protect children against a number of infectious and dangerous diseases. While it’s true that no medical intervention is without risk, the evidence shows that immunization powerfully benefits and protects the community.”²⁹ In May 2015, the Public Policy Institute of California found that 67% of California adults and 65% of public school parents supported not allowing children who have not had the MMR vaccine to attend public schools.³⁰

Despite overwhelming support, the legislation faced strong opposition from some of the public. Hundreds of California parents protested the bill by holding vigils at the Capitol.³¹ Moreover, throughout the year, legislative hearings on the bill attracted outspoken crowds of parents criticizing the legislation. Concerns ranged from the rights of parents to make decisions about their child’s health to the debunked link between vaccinations and autism. Many opponents believe vaccinations are dangerous and contend that parents should be able to make the choice of whether to expose their child to those alleged dangers (none of this is backed by any medical science). The California Coalition for Vaccine Choice, which is organized by those who oppose the bill, argues that “SB 277 eliminates a parent’s right to exempt their children from one, some, or all vaccines, a risk-laden medical procedure including death.”³² The Coalition’s founders and other opponents of the bill say they are currently exploring the possibilities of mounting a legal challenge against the bill.

We believe, though, that this bill does not go far enough. It exempts children from compulsory vaccination if they are home-schooled or educated in off-campus independent study programs. All children should be vaccinated, to protect them and to protect others from the spread of communicable diseases. Even children schooled at home will come into contact with other children and other people, whether at sports events, in parks, or at places like Disneyland. A better approach than the California

<https://www.washingtonpost.com/news/morning-mix/wp/2015/06/26/the-california-assembly-just-approved-one-of-nations-strictest-mandatory-vaccine-laws/> [<https://perma.cc/93SA-KDGL>].

²⁹ Letter from Jerry Brown, Governor of Cal., to the Members of the Cal. State Senate (June 30, 2015), https://www.gov.ca.gov/docs/SB_277_Signing_Message.pdf [<https://perma.cc/PG8M-53NN>].

³⁰ MARK BALDASSARE ET AL., PPIC STATEWIDE SURVEY: CALIFORNIANS AND THEIR GOVERNMENT 13 (2015), http://www.ppic.org/content/pubs/survey/S_515MBS.pdf [<http://perma.cc/23PD-PU4W>].

³¹ Jenna Chandler, *O.C. Parents Protest as Assembly Panel Approves Bill to Require Vaccinations*, ORANGE COUNTY REG. (June 9, 2015, 11:31 PM), <http://www.ocregister.com/articles/parents-665293-bill-sacramento.html> [<http://perma.cc/62U7-6666>].

³² CAL. COALITION FOR VACCINE CHOICE, <http://www.sb277.org> [<http://perma.cc/8MRV-S7E2>].

law would be to require every child to be vaccinated unless there is a medical reason not to do so.

In this Essay, we focus on the constitutional issues concerning compulsory vaccination laws. Our position is that every state should require compulsory vaccination of all children, unless there is a medical reason why the child should not be vaccinated. In other words, there should be no exception to the compulsory vaccination requirement on account of the parents' religion or conscience or for any reason other than medical necessity. Simply put, the government's interest in protecting children and preventing the spread of communicable disease justifies mandatory vaccinations for all children in the United States.

There is no doubt that compulsory vaccination is constitutional. In 1905, in *Jacobson v. Massachusetts*, the Supreme Court held that state compulsory vaccination laws are constitutional when they are "necessary for the public health or the public safety."³³ Since then, the Court has affirmed the constitutionality of state compulsory vaccination laws in cases like *Zucht v. King*, which upheld childhood vaccination requirements for entrance to public schools.³⁴ Indeed, compulsory vaccination laws have existed in the United States in some form since the nineteenth century.³⁵

In Part I of this Essay, we briefly describe the history of compulsory vaccination laws in the United States. Part II explains why such laws are desirable and why every state should require compulsory vaccination with only a medical exception. Finally, Part III looks at the possible constitutional objections based on free exercise of religion and the right of parents to control the upbringing of their children. We conclude that these arguments are not a basis for invalidating compulsory vaccination laws.

I. HISTORY OF COMPULSORY VACCINATION LAWS

In 1796, Dr. Edward Jenner of England became the first physician to develop a vaccination for smallpox by using a system of "deliberate inoculation."³⁶ Not long after, the United States' vaccination movement began in the early nineteenth century and centered on Dr. Benjamin Waterhouse, a physician from Harvard University who had knowledge of Dr. Jenner's work and created a vaccination based on it, and Thomas Jefferson, who strongly supported the widespread delivery of the smallpox

³³ 197 U.S. 11, 27 (1905); see also *infra* notes 98–108 and accompanying text.

³⁴ 260 U.S. 174, 177 (1922); see also *infra* notes 109–14 and accompanying text.

³⁵ James G. Hodge, Jr. & Lawrence O. Gostin, *School Vaccination Requirements: Historical, Social, and Legal Perspectives*, 90 KY. L.J. 831, 849 n.126 (2002).

³⁶ *Id.* at 838–40.

vaccination.³⁷ During this time, vaccination was a resource available only to wealthy Americans because poor communities generally lacked the resources and education to engage in vaccination programs.³⁸ In 1809, however, Massachusetts became the first state to enact a mandatory smallpox vaccination law and government support for compulsory vaccinations began to grow.³⁹

In the mid-nineteenth century, compulsory education laws were enacted in states across the United States. State and local governments grew concerned that the bringing together of school-age children in public schools created a risk of a smallpox outbreak.⁴⁰ In 1827, Boston was the first city to require vaccination records for children upon entering public school.⁴¹ In the years that followed, statewide compulsory vaccination laws for school-age children were enacted in many states, including Massachusetts in 1855, New York in 1862, Connecticut in 1872, Indiana in 1881, Illinois, Arkansas, Virginia, and Wisconsin in 1882, California in 1888, Iowa in 1889, and Pennsylvania in 1895.⁴² The main illness that spurred state compulsory vaccination laws was smallpox. By 1904, “eleven out of then forty-five U.S. states had compulsory vaccination laws.”⁴³

In the following years, the number of states with such laws and the number of required vaccinations grew significantly. By 1980, all fifty states had compulsory vaccination laws that covered children entering public schools for the first time.⁴⁴ By 2003, fifty states required diphtheria and tetanus toxoids and polio, measles, and rubella vaccines. Forty-seven states required the mumps vaccine. Forty-four states required the pertussis

³⁷ See *id.* at 842–43. Jefferson vaccinated his children and servants in 1800 and the following year supported the vaccination of hundreds of his family members, staff, and friends. *Id.*

³⁸ See *id.* at 843.

³⁹ See *id.* at 849 n.126; see also Kevin M. Malone & Alan R. Hinman, *Vaccination Mandates: The Public Health Imperative and Individual Rights*, in *LAW IN PUBLIC HEALTH PRACTICE* 338, 346 (Richard A. Goodman et al. eds., 2d ed. 2007).

⁴⁰ Alfred J. Sciarino, *The Grapes of Wrath, Part II*, 8 J. MED. & L. 1, 17 (2004) (“As a court in Pennsylvania stated in 1916: ‘It is an accepted fact, that during the common school ages, children are specially susceptible to the infectious and contagious diseases mentioned in these acts, and that this hazard is greatly increased by their being brought together from our varied conditions of society. To avoid the spread of these diseases, it has been deemed necessary by the legislature to enforce rigid quarantine and preventive measures, even to the isolation of persons, and exclusion of pupils from infected districts.’” (quoting *Commonwealth v. Gillen*, 65 Pa. Super. 31, 38 (1916))); see also Hodge & Gostin, *supra* note 35, at 850.

⁴¹ Hodge & Gostin, *supra* note 35, at 851.

⁴² *Id.*

⁴³ Kristine M. Severyn, *Jacobson v. Massachusetts: Impact on Informed Consent and Vaccine Policy*, 5 J. PHARMACY & L. 249, 250 (1995).

⁴⁴ Malone & Hinman, *supra* note 39, at 345.

vaccine and the hepatitis B vaccine.⁴⁵ As of 2003, all U.S. states but four—Louisiana, Michigan, South Carolina, and West Virginia—had compulsory vaccination laws covering school-age children from kindergarten to twelfth grade.⁴⁶ These compulsory vaccination laws share two important features: (1) their proven effectiveness in preventing and even eradicating disease and (2) the exemptions to mandatory vaccination that they provide for certain individuals.

By the early 1970s, the Centers for Disease Control and Prevention (CDC) reported that states with compulsory vaccination laws for school-age children experienced a dramatic reduction in measles incidence rates—between 40%–51% lower than states that did not have such laws.⁴⁷ Later that same decade, an analysis conducted as part of the Childhood Immunization Initiative⁴⁸ reported that the incidence rates of measles in states that strictly enforced compulsory vaccination laws were less than one tenth of those in the rest of the country.⁴⁹ Most poignantly, measles outbreaks in Alaska and Los Angeles in 1976 and 1977 “led health officials to strictly enforce the existing requirements” for school-age children.⁵⁰ In Alaska, on the day of the announced crackdown, 8.3% of students, or 7418 students out of 89,109, were excluded from school for failing to meet vaccination requirements.⁵¹ In Los Angeles, approximately 4%, or 50,000 out of 1,400,000, of students were excluded.⁵² One month later, however, only fifty-one students in Alaska remained excluded from school, and in Los Angeles, it only took days for most students to return to school with their required vaccinations.⁵³

Still, within each state’s compulsory vaccination laws, legislators crafted exemptions for certain individuals for different purposes.⁵⁴ For example, all fifty states provide medical exemptions for individuals with contraindicating medical conditions that increase their risk of adverse effect

⁴⁵ *Id.*

⁴⁶ *Id.*

⁴⁷ *Id.* at 344.

⁴⁸ An initiative undertaken in 1977 with the goal of raising childhood vaccination levels to 90% by 1979. *Id.*

⁴⁹ *Id.*

⁵⁰ *Id.*

⁵¹ *Id.*

⁵² *Id.*

⁵³ *See id.*

⁵⁴ *See* CTRS. FOR DISEASE CONTROL & PREVENTION, STATE SCHOOL IMMUNIZATION REQUIREMENTS AND VACCINE EXEMPTION LAWS (2015) [hereinafter SCHOOL VACCINATIONS], <http://www.cdc.gov/phlp/docs/school-vaccinations.pdf> [<https://perma.cc/7WNB-ED7D>].

to a certain vaccine or even multiple vaccines.⁵⁵ Some states—like Connecticut, Montana, and West Virginia—expressly distinguish between whether an exemption is temporary or permanent,⁵⁶ while other states—like Georgia, Kansas, and New Mexico—require recertification⁵⁷ of medical exemptions at different intervals. Though each state’s medical exemption language differs, all states provide such an exemption.⁵⁸

The scope and scale of vaccination exemptions vary by state. In addition to medical exemptions, many states provide religious exemptions and some states provide philosophical exemptions. Five states—Delaware, Iowa, North Carolina, New Jersey, and West Virginia—expressly exclude philosophical exemptions.⁵⁹ For example, Delaware’s law requires an affidavit be signed by those requesting exemption which includes a statement distinguishing what constitutes a religious belief that qualifies for exemption saying, “This belief is not a political, sociological or philosophical view of a merely personal moral code.”⁶⁰ Iowa’s law distinguishes an exemptible religious belief from beliefs that are merely “philosophical, scientific, moral, personal, or medical[ly] oppos[ed] to immunizations.”⁶¹ As of July 2015, only three states—California, Mississippi, and West Virginia—did not have either a religious or philosophical exemption.⁶² Twenty-nine states and the District of Columbia provide only medical and religious exemptions, but not philosophical exemptions from their mandatory vaccination requirements.⁶³

Nonetheless, achieving high vaccination rates remains an important goal for all states. Compiling information in February and March of 2015, the CDC reported that all fifty states and the District of Columbia established vaccination laws for public school children.⁶⁴ Forty-six of those states—excluding only Indiana, Ohio, Michigan, and South Dakota—and the District of Columbia also established vaccination requirements for

⁵⁵ See Malone & Hinman, *supra* note 39, at 348.

⁵⁶ Twenty states distinguish between temporary or permanent according to the CDC’s graph. See SCHOOL VACCINATIONS, *supra* note 54, at 2.

⁵⁷ Nine states require recertification according to the CDC’s graph. See *id.* at 2.

⁵⁸ See Malone & Hinman, *supra* note 39, at 348.

⁵⁹ See SCHOOL VACCINATIONS, *supra* note 54, at 10 app. 2.

⁶⁰ *Id.* at 3 (quoting DEL. CODE ANN. tit. 14, § 131(a)(6) (2016)).

⁶¹ See *id.* (quoting IOWA ADMIN. CODE r. 641-7.3(2) (2016)).

⁶² IMMUNIZATION ACTION COAL., EXEMPTIONS PERMITTED TO SCHOOL AND CHILDCARE IMMUNIZATION REQUIREMENTS (2015), http://www.immunize.org/laws/exemptions_map_july-2015.pdf [<https://perma.cc/XQ4C-5VMP>] (map documenting exemptions).

⁶³ SCHOOL VACCINATIONS, *supra* note 54, at 10 app. 2.

⁶⁴ See *id.* at 7 app. 1 (detailing the statistics cited below).

private school.⁶⁵ All forty-seven of those requirements for private schools mirrored the requirements for public schools.⁶⁶ Additionally, all fifty states and the District of Columbia have vaccination requirements for day care facilities. Forty-four of those states—excluding only Mississippi, Missouri, Montana, Nebraska, Pennsylvania, and West Virginia—and the District of Columbia have requirements for day care facilities that mirror the requirements for public schools.⁶⁷

The 2015 CDC vaccination recommendations for children include a vaccination schedule for fourteen preventable diseases.⁶⁸ The CDC also recommends various vaccinations for preteens, teens, and adults. While states differ on how many of the CDC's vaccination recommendations they adopt into their mandatory vaccination requirements, the number of vaccinations that states require for children remains similar to those mentioned above. The majority of states require vaccinations against diphtheria, polio, measles, mumps, and rubella, varicella, hepatitis B, and pneumococcal viruses for children entering public or private school and day care facilities.⁶⁹ Furthermore, many states also require vaccinations for healthcare workers and patients.⁷⁰

II. COMPULSORY VACCINATION LAWS ARE ESSENTIAL

Many studies demonstrate the enormous value of vaccinations both in terms of preventing death and avoiding needless suffering.⁷¹ An article in the peer-reviewed journal *Pediatrics* concluded that routine childhood immunization will prevent approximately 42,000 early deaths and twenty

⁶⁵ In the four excluded states, the CDC notes the vaccination requirements as “unclear.” *Id.*

⁶⁶ *Id.*

⁶⁷ *Id.*

⁶⁸ See *For Everyone: Easy-to-Read Schedules*, CTRS. FOR DISEASE CONTROL & PREVENTION (2015), <http://www.cdc.gov/vaccines/schedules/easy-to-read/index.html> [<http://perma.cc/UGG9-D82A>] (linking to charts documenting the recommended vaccinations and proper schedule for children 0–6 years old, teens and preteens, and adults).

⁶⁹ See *State Information*, IMMUNIZATION ACTION COALITION, <http://www.immunize.org/laws/> [<http://perma.cc/UQ8R-9GRG>] (linking to maps documenting state coverage of individual vaccinations).

⁷⁰ See *Public Health Law Program*, CTRS. FOR DISEASE CONTROL & PREVENTION, <http://www.cdc.gov/php/publications/topic/vaccinationlaws.html> [<https://perma.cc/KV7Y-WJGZ>].

⁷¹ Vaccinations are now available for the following diseases: haemophilus influenzae type b (Hib), diphtheria, hepatitis A, hepatitis B, influenza, measles, mumps, pertussis (whooping cough), pneumococcal disease, polio, rubella (German measles), tetanus (lockjaw), rotavirus, and varicella (chickenpox). *Vaccines for Children - A Guide for Parents and Caregivers*, U.S. FOOD & DRUG ADMIN, <http://www.fda.gov/BiologicsBloodVaccines/ResourcesforYou/Consumers/ucm345587.htm> [<http://perma.cc/A2XM-M9H3>].

million cases of disease for those born in the year 2009.⁷² Such predictions are consistent with the CDC's reports and findings, which estimated that between 1994 and 2014, 732,000 deaths of U.S. children were prevented, as well as 322 million cases of childhood illnesses due to vaccination.⁷³ Moreover, the American Academy of Pediatrics states that “[m]ost childhood vaccines are 90% to 99% effective in preventing disease.”⁷⁴

Thus, robust evidence lends strong support to our argument that vaccinations are essential to save children's lives. But compulsory vaccinations also are crucial to protect those who cannot be vaccinated, such as infants, and those for whom vaccinations are medically inadvisable, such as those with compromised immune systems. Because there always will be a portion of the population for whom vaccinations will not work, achieving the highest vaccination rates possible for all others remains important. Herd immunity occurs when a “critical portion” of the population—the minimum percentage of vaccinated persons essential to provide herd immunity—is vaccinated against a contagious disease thus creating “little opportunity for an outbreak.”⁷⁵ As a result, members of the community will be protected even if they are not vaccinated or their vaccination does not work.⁷⁶ As Dr. Paul A. Offit explained: “Indeed, when enough people are vaccinated, these infections simply stop spreading.”⁷⁷ Dr. Offit warns that “[f]or highly contagious infections—such as measles or pertussis—the immunization rate needs to be about 95 percent. For somewhat less contagious infections—like mumps and rubella—herd immunity can be achieved with immunization around 85 percent.”⁷⁸ The effects of a decline in herd immunity can be swift. For example, a 2012 outbreak of whooping cough (pertussis) which affected 42,000 people—the largest outbreak since 1955—occurred in an instance where forty-nine

⁷² Fangjun Zhou et al., *Economic Evaluation of the Routine Childhood Immunization Program in the United States*, 2009, PEDIATRICS, Apr. 2014, at 1, 1.

⁷³ Bahar Gholipour, *Vaccination Has Saved 732,000 Children's Lives Since 1994*, LIVE SCIENCE (Apr. 24, 2014, 2:23 PM), <http://www.livescience.com/45111-national-vaccination-effects.html> [<http://perma.cc/68XH-T7NH>].

⁷⁴ AM. ACAD. OF PEDIATRICS, VACCINE SAFETY: THE FACTS 1 (2008), http://www.aap.org/immunization/families/vaccinesafety_parenthandout.pdf [<http://perma.cc/MG2S-CN3Q>].

⁷⁵ See *Community Immunity (“Herd Immunity”)*, U.S. DEP'T OF HEALTH & HUMAN SERVS. (Apr. 16, 2015), <http://www.vaccines.gov/basics/protection/> [<http://perma.cc/VCF9-C3K6>].

⁷⁶ See *id.*

⁷⁷ PAUL A. OFFIT, DEADLY CHOICES: HOW THE ANTI-VACCINE MOVEMENT THREATENS US ALL 145 (rev. foreword 2015 ed. 2011).

⁷⁸ *Id.* at xxiii.

states had dropped below the immunity threshold of 92%–94% as of 2011.⁷⁹

As one commentator noted:

The decline of communal herd immunity is not a merely academic concern. Disease outbreaks have already occurred, killing hundreds and hospitalizing thousands more. “Hot spots” are cropping up in communities across the United States and the rest of the world as well. The rise of exemptions to compulsory vaccination laws threatens to undermine the public health achievements made possible by widespread immunizations.⁸⁰

Given the profound public health threat posed by refusing vaccinations, why are parents placing their children and others at risk? For some parents their anxieties are steeped in medical concerns, others claim to oppose vaccination on religious or philosophical grounds, and for another category of parents, poverty impacts their access to vaccination. It is important then to distinguish between parents who do not vaccinate and those who undervaccinate. For some it is not a choice, but a lack of access to health care. For those parents, frequently the highly mobile and poor, their children often receive some vaccinations, but not all, because of homelessness or frequent moves across cities and states for employment or affordable housing. These parents “undervaccinate,” and are not the population of parents that *refuse* to vaccinate. They, of course, are not the focus of this Essay. In those cases, the solution is to make sure that all have access to vaccinations and the health care system regardless of where they live or their socioeconomic status.

Still other parents may refuse vaccinations based on the fear of the side effects of vaccinations, including fear of autism and even death. Certainly, all drugs expose patients to risks of side effects and vaccinations are no exception, even if clearly on balance they are safe, effective, and the benefits justify the risks. To address potential harms resulting from vaccination, Congress passed the National Childhood Vaccine Injury Act in 1986,⁸¹ which created the National Vaccine Injury Compensation Program (VICP) in 1988.⁸² According to the Health Resources and Services

⁷⁹ Mark Fischetti, *Too Many Children Go Unvaccinated*, SCI. AM. (May 14, 2013), <http://www.scientificamerican.com/article/too-many-children-go-unvaccinated/> [<http://perma.cc/ZM5X-3LK7>].

⁸⁰ Steve P. Calandrillo, *Vanishing Vaccinations: Why Are So Many Americans Opting Out of Vaccinating Their Children?*, 37 U. MICH. J.L. REFORM 353, 421 (2004).

⁸¹ Pub. L. No. 99-660, 100 Stat. 3755 (1986) (codified as amended at 42 U.S.C. §§ 300aa-1 to -34 (2012)).

⁸² *National Vaccine Injury Compensation Program*, U.S. DEP’T OF HEALTH & HUMAN SERVS., HEALTH RES. & SERVS. ADMIN., <http://www.hrsa.gov/vaccinecompensation/index.html> [<http://perma.cc/YUF5-CQ28>]; see also Katherine E. Strong, Note, *Proving Causation Under the*

Administration, “The VICP was established to ensure an adequate supply of vaccines, stabilize vaccine costs, and establish and maintain an accessible and efficient forum for individuals found to be injured by certain vaccines.”⁸³ The VICP replaced the conventional tort system with a no-fault alternative under which the U.S. Court of Federal Claims determines who is compensated.⁸⁴

Yet, the fear of autism remains deeply entrenched among those apprehensive about vaccination.⁸⁵ Dr. Wakefield’s reported link between vaccinations and a greater risk of autism⁸⁶ continues to influence some parents’ decisionmaking, despite *The Lancet*’s retraction and strong repudiation: “[I]t has become clear that several elements . . . are incorrect, contrary to the findings of an earlier investigation.”⁸⁷ The author of the study has since had his medical license revoked.⁸⁸ Many studies conducted in countries all over the world debunk Dr. Wakefield’s finding because none has found any link between vaccinations and autism or anything other than preventing the spread of communicable disease.⁸⁹ Professor Offit notes that in response to the Wakefield paper, six large epidemiological research studies conducted by academic and public health communities all found the vaccines, and specifically thimerosal in them (which Wakefield had pointed to as the causal agent), “didn’t cause autism.”⁹⁰

Yet, many parents, including celebrities,⁹¹ continue to warn the public that vaccinations either cause or expose children to serious risks of developing autism. As one commentator wrote, “Neither the judicial

Vaccine Injury Act: A New Approach for a New Day, 75 GEO. WASH. L. REV. 426, 433–44 (2007) (describing side effects for vaccines and the Act).

⁸³ U.S. DEP’T OF HEALTH & HUMAN SERVS., *supra* note 82.

⁸⁴ *Id.*

⁸⁵ For example, at the debate among Republican presidential candidates in September 2015, Ben Carson, Rand Paul, and Donald Trump were all hesitant to disavow a suggested link between vaccinations and autism. Michael E. Miller, *The GOP’s Dangerous ‘Debate’ on Vaccines and Autism*, WASH. POST (Sep. 17, 2015), <https://www.washingtonpost.com/news/morning-mix/wp/2015/09/17/the-gops-dangerous-debate-on-vaccines-and-autism/> [<https://perma.cc/QSW8-J5HR>].

⁸⁶ Wakefield et al., *supra* note 12.

⁸⁷ Editors of the *Lancet*, *supra* note 12; see also Simon H. Murch et al., Commentary, *Retraction of an Interpretation*, 363 LANCET 750 (2004).

⁸⁸ Alice Park, *Doctor Behind Vaccine-Autism Link Loses License*, TIME (May 24, 2010), <http://healthland.time.com/2010/05/24/doctor-behind-vaccine-autism-link-loses-license/> [<http://perma.cc/E4VB-3RXX>].

⁸⁹ See, e.g., Brent Taylor et al., *Autism and Measles, Mumps, and Rubella Vaccine: No Epidemiological Evidence for a Causal Association*, 353 LANCET 2026 (1999).

⁹⁰ OFFIT, *supra* note 77, at 96.

⁹¹ *Jim Carrey Slams California School Vaccine Legislation: It’s ‘Poisoning More Children,’* HOLLYWOOD REP. (June 30, 2015, 10:56 PM), <http://www.hollywoodreporter.com/news/jim-carrey-slams-school-vaccine-806187> [<http://perma.cc/UR3L-PYQP>].

decisions, the ethics findings, nor *The Lancet's* retraction appear to have shaken the Wakefield faithful.⁹² And as Dr. Paul Offit explained, while “[i]t’s very easy to scare people; it’s very hard to unscare them.”⁹³

Nor has conclusive medical and scientific literature stopped politicians from making statements that have no basis. In 2015, Kentucky Senator Rand Paul, himself a doctor, said that he had delayed his own children’s vaccinations and claimed that there were “many tragic cases of walking, talking, normal children who wound up with profound mental disorders after vaccines.”⁹⁴ Senator Paul cited no medical or scientific literature to back up his claim. None exists. Did Senator Paul’s political ideology cause him to invent “science” and to lose sight of one of the basic tenets of libertarianism: the government can act to prevent people from harming others?

Dr. Paul Offit expressed it well: “We’ve reached a tipping point. Children are suffering and dying because some parents are more frightened by vaccines than by the diseases they prevent. It is time to put an end to this.”⁹⁵ Thus, we propose doing just that. We advocate that every state amend its law to require that every child be vaccinated and that there be no exemptions except where medically necessary.

We turn our attention to those parents who *refuse* vaccinations based on their religious beliefs against medicine⁹⁶ as well as those who aver medical concerns as their reason for avoiding vaccines. As discussed in Part III, there is no constitutional basis for exempting children from vaccinations based on the religious beliefs of their parents. We analyze why compulsory vaccination laws are constitutional.

III. COMPULSORY VACCINATION LAWS ARE CONSTITUTIONAL

In the discussion of the California bill to eliminate religious and conscience exemptions from the compulsory vaccination law, opponents repeatedly asserted that there is a constitutional right of parents to refuse to inoculate their children. The threatened litigation against the law, which

⁹² John Thomas, *Autism, Medicine, and the Poison of Enthusiasm and Superstition*, 7 J. HEALTH & BIOMEDICAL L. 449, 452 (2012).

⁹³ Shirley S. Wang, *Lancet Retracts Study Tying Vaccine to Autism*, WALL ST. J. (Feb. 3, 2010, 12:01 AM), <http://www.wsj.com/articles/SB10001424052748704022804575041212437364420> [<https://perma.cc/QU8U-6TVN>].

⁹⁴ Carrie Dann, *Rand Paul: Vaccines Can Lead to ‘Mental Disorders,’* NBC NEWS (Feb. 2, 2015, 5:07 PM), <http://www.nbcnews.com/politics/elections/rand-paul-vaccines-can-lead-mental-disorders-n298821> [<http://perma.cc/ZF75-UPKV>].

⁹⁵ OFFIT, *supra* note 77, at 191.

⁹⁶ For a discussion of religious beliefs against medicine and their consequences, see PAUL A. OFFIT, *BAD FAITH: WHEN RELIGIOUS BELIEF UNDERMINES MODERN MEDICINE* (2015).

seems likely to occur, will be on constitutional grounds.⁹⁷ Rhetorically, of course, claiming that a bill is unconstitutional is a powerful argument. Also, there is no doubt that opponents of compulsory vaccination sincerely believe that parents have a constitutional right to refuse to vaccinate their children.

They are wrong. No such constitutional right exists. In fact, every court to consider challenges to compulsory vaccination laws has upheld the statutes. In this Part, we initially review those cases. We then explain why neither the claimed right of religious freedom nor the asserted right of parents to control the upbringing of their children justifies a constitutional exemption from compulsory vaccination requirements.

A. Courts Have Consistently Rejected Constitutional Challenges to Compulsory Vaccination Laws

The Supreme Court has twice considered constitutional challenges to state laws requiring compulsory vaccination and in both instances rejected the challenges and upheld the laws. Most famously, in *Jacobson v. Massachusetts*, the Court upheld a Massachusetts law that required compulsory smallpox vaccinations for adults.⁹⁸ This case took place during a time when smallpox was a very real and immediate threat to the population of Massachusetts.⁹⁹

The Court held that laws promoting public health or safety fall under a state's police power and are under the sole discretion of the state unless the law violates the Constitution.¹⁰⁰ Additionally, individual rights may need to yield to the state's police power in order to preserve the public health or safety. "There are manifold restraints to which every person is necessarily subjected for the common good."¹⁰¹

The Court then found that the Massachusetts legislature and the Board of Health had the discretion to enact compulsory vaccination when such vaccination is necessary for the public health or safety.¹⁰² The Court explained that smallpox was "prevalent and increasing" in Cambridge, Massachusetts, and, therefore, compulsory vaccination appeared a

⁹⁷ See *Could Proposed Mandatory Vaccine Laws Survive Legal Challenges?*, HEALTH IMPACT NEWS: VACCINE IMPACT (Dec. 5, 2015), <http://vaccineimpact.com/2015/could-proposed-mandatory-vaccine-laws-survive-legal-challenges/> [<http://perma.cc/J2JS-HREN>].

⁹⁸ 197 U.S. 11, 27 (1905).

⁹⁹ *Id.* at 29–31 (referring to smallpox as an "imminent danger" that "imperilled an entire population").

¹⁰⁰ *Id.* at 25.

¹⁰¹ *Id.* at 26.

¹⁰² See *id.* at 27.

necessity to protect the public health and safety.¹⁰³ Because the law was enacted to combat smallpox, the means prescribed by Massachusetts did have a “real [and] substantial relation to the protection of the public health and the public safety.”¹⁰⁴

The Court also held that skepticisms about the efficacy of vaccinations against diseases among the public or some physicians does not mean that a state legislature cannot enact a compulsory vaccination law.¹⁰⁵ The Court found that the common belief among physicians and the public was that vaccinations do prevent the spread of disease and this common belief was enough to justify the legislature’s actions.

The defendant argued that vaccinations could be harmful and that it would be impossible to tell in an individual case whether a vaccination would be beneficial at all.¹⁰⁶ The Court held that because the defendant could not prove that he was in the class of people who were medically unfit for receiving vaccinations, his argument was not persuasive.¹⁰⁷ The Court noted that this case did not concern an adult who would be harmed by a vaccine. According to the Court, this

[was] the case of an adult who, for aught that appears, was himself in perfect health and a fit subject of vaccination, and yet, while remaining in the community, refused to obey the statute and the regulation adopted in execution of its provisions for the protection of the public health and the public safety, confessedly endangered by the presence of a dangerous disease.¹⁰⁸

In a less well known, but equally important decision, *Zucht v. King*, the Court held that a city can impose compulsory vaccination for all children in school, even if there is no immediate threat of an epidemic like there was in *Jacobson*.¹⁰⁹ In that case, San Antonio, Texas, ordinances required that “no child or any other person shall attend a public school or other place of education without having first presented a certificate of vaccination.”¹¹⁰ Under these ordinances, “public officials excluded Rosalyn Zucht from a public school because she did not have the required certificate

¹⁰³ See *id.* at 28.

¹⁰⁴ *Id.* at 31.

¹⁰⁵ See *id.* at 34–35.

¹⁰⁶ See *id.* at 36.

¹⁰⁷ See *id.* at 36–37.

¹⁰⁸ *Id.* at 39.

¹⁰⁹ 260 U.S. 174 (1922).

¹¹⁰ *Id.* at 175.

and refused to submit to vaccination.”¹¹¹ Public officials also excluded her from private school.

Rosalyn’s parents then brought a suit against the officials in state court. Rosalyn claimed

that there was then no occasion for requiring vaccination; that the ordinances deprive plaintiff of her liberty without due process of law by, in effect, making vaccination compulsory; and, also, that they are void because they leave to the Board of Health discretion to determine when and under what circumstances the requirement shall be enforced without providing any rule by which that board is to be guided in its action and without providing any safeguards against partiality and oppression.¹¹²

The Supreme Court rejected these arguments and held that “the municipality may vest in its officials broad discretion in matters affecting the application and enforcement of a health law.”¹¹³ The Court declared that “these ordinances confer not arbitrary power, but only that broad discretion required for the protection of the public health.”¹¹⁴ Therefore, the Court held that a state can constitutionally impose a compulsory vaccination requirement for school children.

These decisions should put an end to arguments that compulsory vaccination laws are unconstitutional. Not surprisingly, all subsequent challenges to such state statutes have been rejected by both federal and state courts.

For example, in *Workman v. Mingo County Board of Education*, the United States Court of Appeals for the Fourth Circuit held that a West Virginia law requiring all school children to be vaccinated, with no exemption for religious reasons, is constitutional.¹¹⁵ The court explained that compulsory vaccination laws are within the state’s police power, even though there may not be an immediate threat of disease. The court of appeals said that Supreme Court has settled that claims of religious freedom must yield to the compelling social interest of combating the spread of disease through mandatory immunization programs.

The court of appeals rejected the parents’ claim of a religious right to not vaccinate their children by citing to *Prince v. Massachusetts*,¹¹⁶ and its holding that “[t]he right to practice religion freely does not include liberty to expose the community or the child to communicable disease or the latter

¹¹¹ *Id.*

¹¹² *Id.*

¹¹³ *Id.* at 176.

¹¹⁴ *Id.* at 177.

¹¹⁵ 419 F. App’x 348 (4th Cir. 2011).

¹¹⁶ 321 U.S. 158 (1944).

to ill health.”¹¹⁷ The court said that *Jacobson*’s holding is not limited to diseases that present an immediate danger.¹¹⁸ The Fourth Circuit thus concluded that “the West Virginia statute requiring vaccinations as a condition of admission to school [did] not unconstitutionally infringe Workman’s right to free exercise.”¹¹⁹

Many other federal courts have come to similar conclusions. In *McCarthy v. Boozman*, a federal district court upheld the Arkansas compulsory vaccination law and declared: “The constitutional right to freely practice one’s religion does not provide an exemption for parents seeking to avoid compulsory immunization for their school-aged children.”¹²⁰ In *Sherr v. Northport–East Northport Union Free School District*, a federal district court upheld the New York law and stated: “[I]t has been settled law for many years that claims of religious freedom must give way in the face of the compelling interest of society in fighting the spread of contagious diseases through mandatory inoculation programs.”¹²¹

State courts faced with the issue have come to the identical conclusion. In *Wright v. DeWitt School District*, the Arkansas Supreme Court held that it is within the state’s police power “to require that school children be vaccinated and that such requirement does not violate the constitutional rights of anyone, on religious grounds or otherwise.”¹²²

In fact, some courts have held that religious exemptions to compulsory vaccination laws are unconstitutional because they impermissibly favor religion.¹²³ In *Brown v. Stone*, the Mississippi Supreme Court held that a religious exemption in the Mississippi state compulsory vaccination law for school children was unconstitutional because it only allowed members of recognized denominations to obtain exemption.¹²⁴ The court concluded that because a state compulsory vaccination law could stand on its own without a religious exemption, the law was constitutionally valid without the exemption.

¹¹⁷ 419 F. App’x at 353 (quoting *Prince*, 321 U.S. at 166–67).

¹¹⁸ *Id.*

¹¹⁹ *Id.* at 353–54.

¹²⁰ 212 F. Supp. 2d 945, 948 (W.D. Ark. 2002).

¹²¹ 672 F. Supp. 81, 88 (E.D.N.Y. 1987).

¹²² 385 S.W.2d 644, 646 (Ark. 1965); see also *Cude v. State*, 377 S.W.2d 816, 819 (Ark. 1964) (“According to the great weight of authority, it is within the police power of the State to require that school children be vaccinated against smallpox, and that such requirement does not violate the constitutional rights of anyone, on religious grounds or otherwise.”).

¹²³ For development of this argument, see Allan J. Jacobs, *Do Belief Exemptions to Compulsory Vaccination Programs Violate the Fourteenth Amendment?*, 42 U. MEM. L. REV. 73 (2011).

¹²⁴ 378 So. 2d 218, 223 (Miss. 1979).

The Mississippi Supreme Court found:

[T]he statute in question, requiring immunization against certain crippling and deadly diseases particularly dangerous to children before they may be admitted to school, serves an overriding and compelling public interest, and that such interest extends to the exclusion of a child until such immunization has been effected, not only as a protection of that child but as a protection of the large number of other children comprising the school community and with whom he will be daily in close contact in the school room.¹²⁵

Compulsory vaccinations are so important for protecting our children and the community against dangerous diseases that “[t]o the extent that it may conflict with the religious beliefs of a parent, however sincerely entertained, the interests of the school children must prevail.”¹²⁶

Further, the court concluded:

We have no difficulty here in deciding that the statute is “complete in itself” without the provision for religious exemption and that it serves a compelling state interest in the protection of school children. Therefore, we hold that the provision providing an exception from the operation of the statute because of religious belief is in violation of the Fourteenth Amendment to the United States Constitution and therefore is void.¹²⁷

Because the statute can stand on its own, the rest of it is constitutionally valid and can continue as law. Therefore, only the religious exemption was struck down.

Similarly, in *Davis v. State*, the Maryland Court of Appeals held that the state’s religious exemption clause in its compulsory vaccination statute violated the establishment clause of the First Amendment because it only allowed exemption for children whose parents were members of a recognized church or denomination.¹²⁸ Moreover, the court held that the religious exemption clause was severable from the rest of the statute because compulsory vaccination statutes do not need religious exemption clauses.¹²⁹

Thus, the cases from courts at all levels and from all jurisdictions are unanimous: state laws requiring compulsory vaccination are constitutional. The following Sections more carefully examine the constitutional objections to compulsory vaccination laws.

¹²⁵ *Id.* at 222–23.

¹²⁶ *Id.* at 223.

¹²⁷ *Id.*

¹²⁸ 451 A.2d 107, 113 (Md. 1982).

¹²⁹ *Id.* at 115.

B. The Objection Based on Religious Freedom

A frequent objection to compulsory vaccination laws is that they intrude on the right of parents to practice their religion. Parents who oppose medical care on religious grounds contend that their beliefs require a constitutional exemption from mandatory inoculation requirements. Under current First Amendment law this claim is groundless, without even needing to consider whether the state has a sufficient interest in requiring vaccinations.

In 1990, in *Employment Division v. Smith*, the Court held that the Free Exercise Clause cannot be used to challenge a neutral law of general applicability.¹³⁰ In other words, no matter how much a law burdens religious practices, it is constitutional under *Smith* so long as it does not single out religious behavior for punishment and was not motivated by a desire to interfere with religion.

Smith involved a challenge by Native Americans to an Oregon law prohibiting use of peyote, a hallucinogenic substance. Specifically, individuals challenged the state's determination that their religious use of peyote, which resulted in their dismissal from employment, was misconduct disqualifying them from receipt of unemployment compensation benefits.¹³¹

Justice Scalia, writing for the majority, rejected the claim that free exercise of religion required an exemption from an otherwise valid law. Justice Scalia said that “[w]e have never held that an individual’s religious beliefs excuse him from compliance with an otherwise valid law prohibiting conduct that the State is free to regulate. On the contrary, the record of more than a century of our free exercise jurisprudence contradicts that proposition.”¹³² Justice Scalia thus declared “that the right of free exercise does not relieve an individual of the obligation to comply with a ‘valid and neutral law of general applicability on the ground that the law proscribes (or prescribes) conduct that his religion prescribes (or proscribes).’”¹³³

The Court stressed that it should be the political process, and not the judicial, that provides for exemptions in laws to protect religious beliefs. Justice Scalia said that:

Precisely because “we are a cosmopolitan nation made up of people of almost every conceivable religious preference,” and precisely because we value and

¹³⁰ 494 U.S. 872 (1990).

¹³¹ *Id.* at 874.

¹³² *Id.* at 878–79.

¹³³ *Id.* at 879 (quoting *United States v. Lee*, 455 U.S. 252, 263 n.3 (1982) (Stevens, J., concurring)).

protect that religious divergence, we cannot afford the luxury of deeming *presumptively invalid*, as applied to the religious objector, every regulation of conduct that does not protect an interest of the highest order.¹³⁴

The Court said that those seeking religious exemptions from laws should look to the democratic process for protection, not the courts.

There is no doubt that *Smith* changed the test for the free exercise clause. No longer is strict scrutiny used when the challenge is to a neutral law of general applicability. Such laws are upheld so long as they meet a deferential rational basis test. This applies to vaccination. State statutes requiring vaccinations of all children are neutral laws of general applicability. They are not motivated by a desire to interfere with religion and they apply to everyone. Therefore, there is no basis for a First Amendment challenge to compulsory vaccination laws.

In response to *Smith*, Congress adopted two statutes to restore religious freedom rights by statute. Neither provides a basis for challenging compulsory vaccination laws.

Congress adopted the Religious Freedom Restoration Act of 1993 to restore the law to what it was before *Smith*: strict scrutiny for claims that the government is significantly burdening religion, even when it is a challenge to a neutral law of general applicability.¹³⁵ The Act declares that its purpose is “to restore the compelling interest test . . . and to guarantee its application in all cases where free exercise of religion is substantially burdened; and . . . to provide a claim or defense to persons whose religious exercise is substantially burdened by government.”¹³⁶ The key provision of the Act states:

Government shall not substantially burden a person’s exercise of religion even if the burden results from a rule of general applicability, except . . . [g]overnment may substantially burden a person’s exercise of religion only if it demonstrates that application of the burden to the person . . . (1) is in furtherance of a compelling governmental interest; and (2) is the least restrictive means of furthering that compelling governmental interest.¹³⁷

However, the Supreme Court quickly declared the Religious Freedom Restoration Act unconstitutional as applied to state and local governments. In *City of Boerne v. Flores*, a 6–3 decision, the Court held that the law was unconstitutional as exceeding the scope of Congress’s powers under

¹³⁴ *Id.* at 888 (citation omitted) (quoting *Braunfeld v. Brown*, 366 U.S. 599, 606 (1961)).

¹³⁵ See Pub. L. No. 103-141, 107 Stat. 1488 (1993) (codified at 5 U.S.C. § 504, 42 U.S.C. §§ 1988, 2000bb to 2000bb-4 (2012)), *invalidated in part by* *City of Boerne v. Flores*, 521 U.S. 507 (1997).

¹³⁶ § 2(b) (citations omitted).

¹³⁷ § 3(a)–(b).

Section Five of the Fourteenth Amendment. Justice Kennedy, writing for the majority, stated that Section Five empowers Congress to enact laws “to enforce” the amendment, but Congress is not “enforcing” when it creates new constitutional rights or expands the scope of rights.¹³⁸ The Court held that Congress under Section Five may act only to prevent or remedy the violation of rights recognized by the courts. Such laws must be narrowly tailored; they must be proportionate and congruent to prevent and remedy the constitutional violations.¹³⁹ The Religious Freedom Restoration Act was deemed to fail these requirements and was declared unconstitutional as applied to state and local governments. It therefore cannot be used to challenge state laws requiring vaccinations.

In 2000, in response to *City of Boerne v. Flores*, the Religious Land Use and Institutionalized Persons Act was adopted by Congress.¹⁴⁰ This law requires that the government meet strict scrutiny when it significantly burdens religion in two areas: land use decisions and institutionalized persons. Congress justified acting to regulate land use decisions under its commerce power and to regulate institutionalized persons under its spending power as a condition on federal funds. But state laws requiring vaccinations do not involve either of these areas, so this statute is inapplicable as a basis for challenges.

Thus, under current law, there is no basis for a religious challenge—either under the Constitution or federal laws—to state laws’ mandatory vaccinations for all children.

C. Compulsory Vaccination Laws Meet Strict Scrutiny

In addition to claims of free exercise of religion, parents also challenge mandatory inoculation requirements on the ground that it infringes their constitutional right as parents to control the upbringing of their children. The Court has recognized this as a fundamental right protected under the word “liberty” of the Due Process Clause.

In *Meyer v. Nebraska*, in 1923, the Supreme Court declared a state law unconstitutional that prohibited teaching in any language other than English in the public schools.¹⁴¹ The Court invalidated the law, not on First Amendment grounds, but by using substantive due process and finding that

¹³⁸ See *Flores*, 521 U.S. at 519. For a criticism of this aspect of *City of Boerne v. Flores*, see Erwin Chemerinsky, *The Religious Freedom Restoration Act Is a Constitutional Expansion of Rights*, 39 WM. & MARY L. REV. 601 (1998).

¹³⁹ *Flores*, 521 U.S. at 514, 520.

¹⁴⁰ Pub. L. No. 106-274, 114 Stat. 803 (2000) (codified at 42 U.S.C. §§ 2000cc to 2000cc-5 (2012)).

¹⁴¹ 262 U.S. 390, 403 (1923).

the statute violated the right of parents to make decisions for their children.¹⁴² Similarly, two years later, in *Pierce v. Society of Sisters*, the Supreme Court held unconstitutional a state law that required children to attend public schools.¹⁴³ The Court explained that:

The fundamental theory of liberty upon which all governments in this Union repose excludes any general power of the state to standardize its children by forcing them to accept instruction from public teachers only. The child is not the mere creature of the State; those who nurture him and direct his destiny have the right, coupled with the high duty, to recognize and prepare him for additional obligations.¹⁴⁴

Fifty years later, in *Wisconsin v. Yoder*, the Supreme Court held that Amish parents had a constitutional right, based on their right to control the upbringing of their children and based on free exercise of religion, to exempt their 14- and 15-year-old children from a compulsory school attendance law.¹⁴⁵ The Court said that:

[A] State's interest in universal education, however highly we rank it, is not totally free from a balancing process when it impinges on fundamental rights and interests, such as those specifically protected by the Free Exercise Clause of the First Amendment, and the traditional interest of parents with respect to the religious upbringing of their children.¹⁴⁶

The Court gave great weight to the parents' claim that additional education would threaten their children's religious beliefs and to the uniquely insulated nature of the Amish culture. The Court accepted the argument that applying the mandatory schooling law to 14- and 15-year-old Amish children would interfere with free exercise of religion and with the ability of parents to make decisions concerning their children. The Court noted that there was no evidence of "any harm to the physical or mental health of the child or to the public safety, peace, order, or welfare."¹⁴⁷ The Court thus concluded that "[u]nder the doctrine of *Meyer v. Nebraska*, . . . we think it entirely plain that the Act . . . interferes with the liberty of

¹⁴² In part, this is because the First Amendment had not yet been incorporated into the Fourteenth Amendment and applied to the states. See *Gitlow v. New York*, 268 U.S. 652, 666 (1925) (finding that the First Amendment applies to the states through its incorporation into the Due Process Clause of the Fourteenth Amendment).

¹⁴³ 268 U.S. 510 (1925).

¹⁴⁴ *Id.* at 535.

¹⁴⁵ 406 U.S. 205, 207-08 (1972).

¹⁴⁶ *Id.* at 214.

¹⁴⁷ *Id.* at 230.

parents and guardians to direct the upbringing and education of children under their control.”¹⁴⁸

The Supreme Court most recently considered the right of parents to control the upbringing of their children in the context of a state law protecting grandparents’ rights. In *Troxel v. Granville* the Supreme Court declared unconstitutional Washington’s grandparent visitation law as violating the right of parents to control the upbringing of their children.¹⁴⁹ Justice O’Connor’s plurality opinion began by noting the fundamental nature of the right involved: “The liberty interest at issue in this case—the interest of parents in the care, custody, and control of their children—is perhaps the oldest of the fundamental liberty interests recognized by this Court.”¹⁵⁰ The plurality found that the Washington law, as applied in this case, was unconstitutional as infringing on this fundamental right.

There is thus a stronger claim that state laws requiring compulsory vaccination infringe the right of parents to control the upbringing of their children than there is an argument that such laws infringe free exercise of religion. However, and quite significantly, the Court also has recognized that the right to make parenting decisions is not absolute and can be interfered with by the state if necessary to protect a child. For example, in *Prince v. Massachusetts*, the Court upheld the application of child labor laws to a nine-year-old girl who was soliciting for the Jehovah’s Witnesses religion at the direction of her parents.¹⁵¹

In *Prince*, the Court acknowledged that there is a “private realm of family life which the state cannot enter.”¹⁵² But the Court also opined that:

[T]he family itself is not beyond regulation in the public interest Acting to guard the general interest in youth’s well being, the state as *parens patriae* may restrict the parent’s control by requiring school attendance, regulating or prohibiting the child’s labor and in many other ways.¹⁵³

The Court observed that the need to protect children from being exploited and harmed justified upholding laws prohibiting child labor, even if the work was at the direction of the parents and even if it was undertaken for religious purposes.¹⁵⁴

¹⁴⁸ *Id.* at 232–33 (quoting *Pierce*, 268 U.S. at 534–35).

¹⁴⁹ 530 U.S. 57, 72–73 (2000).

¹⁵⁰ *Id.* at 65.

¹⁵¹ 321 U.S. 158 (1944).

¹⁵² *Id.* at 166.

¹⁵³ *Id.* (footnotes omitted).

¹⁵⁴ The free exercise aspect of this case is discussed in ERWIN CHERMERINSKY, CONSTITUTIONAL LAW: PRINCIPLES AND POLICIES § 12.3.2 (5th ed. 2015).

State laws that require compulsory vaccination of all children, except when there is a medical reason to not inoculate, meet strict scrutiny. The government has a compelling interest in protecting children from communicable diseases, which could kill or seriously injure them. In fact, courts across the country have consistently held that states can require medical care that potentially could save a child's life, even when the parents object on religious or other grounds.¹⁵⁵ As we emphasize in this Essay, the government also has a compelling interest in protecting others from the spread of communicable diseases. For example, infants and those who cannot be vaccinated for medical reasons need the rest of the population to be vaccinated in order to be protected from communicable diseases.¹⁵⁶

Strong and irrefutable medical and scientific evidence demonstrates that there is no less restrictive alternative except to require every person to be vaccinated. Only vaccinations can protect children from communicable diseases. Only by vaccinating every child who medically can be inoculated, can there be protection for those who cannot be vaccinated, whether by reason of being too young or it being medically inadvisable.

In other words, compulsory vaccination laws meet strict scrutiny. As demonstrated in this Essay, that is why every court to consider them has deemed compulsory vaccination to be constitutional.

CONCLUSION

Claims of personal freedom understandably and deservedly carry great weight in our society. But one of the most basic principles of liberty is that a person's freedom does not justify infringing injury on others. Those who fail to vaccinate their children are unnecessarily risking that their children will be exposed to communicable diseases that can have serious or even fatal consequences. Those not vaccinated also can spread communicable diseases to others in society who cannot be vaccinated.

¹⁵⁵ See, e.g., *Walker v. Superior Court*, 763 P.2d 852, 855 (Cal. 1988) (“[A] prosecution for involuntary manslaughter and felony child endangerment can be maintained against the mother of a child who died of meningitis after receiving treatment by prayer in lieu of medical attention.” (citations omitted)); *People v. Rippberger*, 283 Cal. Rptr. 111 (Cal. Ct. App. 1991) (noting the free exercise of religion does not mean that a parent can engage in conduct that is life-threatening to his or her child, and therefore a parent is liable if he or she utilizes prayer treatment instead of medical treatment and thus causes the child harm or death); *In re McCauley*, 565 N.E.2d 411 (Mass. 1991) (finding it is appropriate for a state to order medical treatment for a sick child over a parent's religious objections; although parents' rights over their children and religious rights are important, those rights must yield to the state's interest in keeping a child alive when that child is dangerously ill).

¹⁵⁶ See *supra* Part II.

Our conclusion is that laws that require vaccination need not—and should not—have exceptions for religion or for conscience. Compulsory vaccination laws are unquestionably constitutional without such exceptions. Indeed, we urge every state to revise its vaccination law to make sure that every child, and every person, is vaccinated unless there is a medical reason not to do so.

