

Geospatial Distribution of MMR Vaccination and Incidence in Iraq, 2001-2016

Haley Comfort

A thesis

submitted in partial fulfillment of the
requirements for the degree of

Master of Public Health

University of Washington

2019

Committee:

Herbert Duber

Amy Hagopian

Program Authorized to Offer Degree:

Global Health

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Abstract

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Haley Comfort

Chair of the Supervisory Committee:

Herbert Duber

Department of Global Health

The 2003 U.S.-led invasion of Iraq created health system instability, with direct and indirect public health consequences. This analysis examines the disparity in vaccine coverage, incidence, and displacement in Iraq at the governorate level for three vaccine-preventable diseases – measles, mumps, and rubella – between 2001 and 2016 using data from the Iraqi Ministry of Health and annual totals of persons of concern from the United Nations High Commissioner for Refugees. We first performed descriptive analyses to look at the geospatial variation of reported vaccine coverage and disease incidence, identifying large variability in incidence of the three diseases – on the order of 100x for measles - between governorates. In a pooled statistical analysis, using a linear mixed effects regression model, we saw an increase in incident measles cases per 100,000 persons for each additional percent unvaccinated (0.8, 95% CI: [0.4, 1.2], p-value < 0.001). Analyzing governorates individually, the statistically significant estimates varied between 1.6 to 3.7 additional cases per 100,000 persons. When incorporating persons of concern into our pooled regression model, we identified larger measles incidence for every additional

10,000 persons of concern (0.26, 95% CI: [0.19, 0.33], p-value < 0.001), holding vaccine coverage constant. These relationships were not significant for mumps or rubella. In conclusion, we found high variability in the geospatial pattern of MMR vaccine coverage and disease incidence between 2001 and 2016 that was not adequately captured by the national level summary statistics. However, the relationship between incidence and vaccine coverage is complex and complicated by other factors, so we did not expect a consistent association between the two variables.

Introduction

The invasion of Iraq began March 20, 2003, and within one month, American and British troops had spread throughout the country.¹ In that short time, instability caused by the conflict devastated the health system, thereby disrupting the Iraqi population's ability to access health care. By June, approximately 210,000 children had been unable to receive necessary vaccinations after birth.²

The Iraqi Ministry of Health (Iraq MoH) and humanitarian groups endeavored to maintain adequate amounts of supplies, ensure equipment worked along the cold chain to preserve vaccines, and sustain programs that provided preventative health care to the population, especially children.^{2,3,4} These humanitarian groups also coordinated vaccination campaigns to administer the measles, mumps, and rubella (MMR) vaccine to vulnerable populations throughout the country or in key areas.⁵

A recent analysis of communicable disease incidence by Zhao et al. provides insights into national trends of vaccine-preventable disease in the post-invasion years.⁶ Outbreaks of measles, mumps, and rubella were observed, with 30,321 measles cases in 2009, 12,815 and 74,212 mumps cases in 2004 and 2016, respectively, and 290 rubella cases in 2004. Further analysis performed by Lafta and Hussain examined the relationship between national vaccine coverage and outbreaks of vaccine-preventable illness, finding that fluctuations in vaccine coverage precipitated outbreaks.⁷ They also described a secular trend for measles which peaked every four to five years.⁷

However, analyses to date have not examined subnational data. A governorate-level geospatial analysis can better identify disparities across smaller geographies and assess the effectiveness of interventions which can be missed when examining only national-level trends. These types of analyses are also important for surveillance because they can help identify any common trends that occur prior to the initiation of major outbreaks. Public health planning and implementation of new programs then can address the concerns.

In this study, we examine a subnational-level time series of three key vaccine preventable diseases – measles, mumps, and rubella – in Iraq from 2001 to 2016 by looking at incidence and

vaccine coverage for the measles, mumps, and rubella (MMR) vaccine. We also assess additional risk factors for a disease outbreak at the subnational level that may contribute to variability in the relationship of interest. These include annual population change and the annual number of “persons of concern” (internally displaced persons and refugee migrants, mostly) residing in each governorate. We believe that by examining vaccine coverage as an indicator of incidence and by incorporating additional variables representing large migration and vulnerability among populations, this analysis will help to explain why outbreaks spread to some areas and not others.



Figure 1: Map of Iraqi Governorates

Methods

Study Design

The primary dataset for this study comes from the Ministry of Health in Iraq. The dataset maintains records at the governorate level for 32 communicable diseases across four broad categories: 1) vaccine-preventable diseases, 2) other World Health Organization (WHO) surveillance diseases, 3) other vector-borne and zoonotic diseases, and 4) reemerging diseases.⁶ Data is collected on a monthly basis for notifiable vaccine-preventable diseases from each Iraqi governorate. Per Iraq MoH policy, all public-sector hospitals and primary health care centers reported their monthly case totals to the Preventive Health Department in the Directorate General of Health for their respective governorate. This data is then reported to the Communicable Disease Control Unit of the Ministry of Health in Iraq. The dataset also includes variables for governorate-level population and vaccine coverage.

Our analysis of this dataset explores the vaccine-preventable diseases category by examining the three diseases prevented by the MMR vaccine – measles, mumps, and rubella – at the governorate level between 2001 and 2016. Vaccine coverage is measured as the percent vaccinated among children under 5 years of age.

We used a supplemental dataset from The United Nations High Commissioner for Refugees (UNHCR) entitled “Demographics for UNHCR's populations of concern residing in Iraq” to incorporate a measure of annual vulnerability.⁹ UNHCR defines ‘persons of concern’ as refugees (people fleeing conflict or persecution from another country), returnees, stateless people, internally displaced Iraqis, and asylum seekers.¹⁰ This dataset reports yearly totals for the number of person of concern in various areas across Iraq from 2005 to 2016.

Data Management

We calculated disease incidence per 100,000 persons using the equation: $incidence = \frac{\# \text{ cases}}{\text{population}} \times 100,000$. The figures in Appendix A show incidence and cases counts for measles, mumps, and rubella at the governorate-level between 2001 and 2016.

We used the percent vaccinated variable among children under 5 years of age in the Iraq MoH dataset to determine the percent unvaccinated by subtracting percent vaccinated from 100. Using percent unvaccinated better highlights which governorates had the greatest need for vaccines throughout the time period. Appendix A also illustrates MMR coverage between 2001 and 2016. The cutoffs chosen for these bins represent the common thresholds of recommendations for herd immunity of 99% vaccinated, 95% vaccinated, and 90% vaccinated as well as lower coverage values of 85% vaccinated, 75% vaccinated, and 50% vaccinated since vaccine coverage in some governorates dropped to dangerously low levels.¹¹ We also calculated governorate-level change in vaccine coverage by subtracting each year's percent vaccinated from the following year. This showed the absolute change, or difference in percentage points, from one year to the next, allowing the maps in Figure 1 (Appendix B) to illustrate whether coverage dropped or increased in each governorate.

To acknowledge and incorporate the large variation in population size between governorates, we measured relative population change, rather than calculating a cruder absolute population change. We transformed governorate-level population counts in the Iraq MoH dataset to create new variables. We calculated population density by dividing the governorate-level population total by the area (miles²) for the corresponding governorate.¹² We calculated percent population change using the equation: $\% \text{ change} = \frac{\text{year}_{x+1} - \text{year}_x}{\text{year}_x} * 100$ to show when governorates had stable population compared to times of significant movement into or out of a governorate. This variable is shown in Figure 2 (Appendix B).

An important component of population change is the number of persons of concern. The dataset from UNHCR with this information had to be cleaned. We edited cities and alternative spellings of governorate names for consistency or reassigned to the correct governorate. We summed sex-specific totals for each governorate by year from 2005 to 2016 which we show in Figure 3 (Appendix B). About 120,000 persons of concern had to be removed from the dataset due to unknown locations or their assignment to "No Man's Land" (unoccupied or disputed land).

We used R (version 3.5.0) for data cleaning, correction, and analysis. We merged the IMoH dataset with shapefiles of the administrative level 1 (governorate-level) boundaries acquired from the Humanitarian Data Exchange website.¹³ We created maps using the *ggplot2* package.

Analysis

We conducted statistical and descriptive analyses to examine the relationship between annual disease incidence and vaccine coverage.

The descriptive analysis explains trends seen in incidence and vaccine coverage from 2001 to 2016. Additional factors, population change and the number of persons of concern residing in each governorate, potentially affecting both these variables, are also described.

We performed a regression analysis to produce a pooled estimate of the risk difference for the relationship of interest between vaccine coverage and incidence. We ran a linear mixed-effects model with disease incidence per 100,000 as the dependent variable and vaccine coverage as the independent variable. We also included governorate as a fixed effect term to control for correlation in incidence within governorates. For this analysis, we offset the vaccine coverage variable by two years prior to account for outbreaks which started and rolled into the year reporting the main outbreak.

We ran a similar analysis of vaccine coverage and disease incidence per 100,000 for each governorate to gather unpooled estimates of this relationship. This linear regression model had the same variables as the linear mixed-effects model, but it did not include a fixed effect term to control for governorate.

To compare whether the regression coefficients from the pooled analysis and statistically significant governorate-level estimates were equal, we conducted a Z-test using the equation:

$$Z = \frac{\beta_{pooled} - \beta_{unpooled\ subnational}}{\sqrt{(SE\beta_{pooled})^2 + (SE\beta_{unpooled\ subnational})^2}} .$$
 The resulting Z-scores depict the number of standard

deviations between the pooled and unpooled subnational risk difference estimates.

To identify whether an interaction between vaccine coverage and the number of persons of concern exists, we ran an additional version of our pooled linear mixed effects regression model which included an interaction term for this relationship of interest. For this model, we used a subsetted version of our data which started in 2005 and included only the governorates and years when governorates reportedly hosted persons of concern.

Results

Incidence of Measles, Mumps, and Rubella

The incidences calculated from the Iraq MoH dataset depict a major outbreak of measles in Iraq from 2008 to 2009. During that time, 11 of the 18 governorates reported their highest incidence between 2001 and 2016. While ten governorates reported incidences near or less than 60 per 100,000 persons, eight governorates reported incidences larger than 120 per 100,000. Dahuk reported the smallest incidence of 3.9 per 100,000 and Wassit reported the largest incidence 379.3 per 100,000. It appears that the governorates with decreasing vaccine coverage in 2007 experienced a higher incidence of measles the following year in 2008 that spread quickly and rolled into 2009. While the efforts of the containment operations which responded after identifying the outbreak in 2008 likely prevented the outbreak from spreading further by increasing vaccine coverage, the outbreak still infected many vulnerable individuals (30,321 cases total in 2009).¹⁴ A smaller outbreak of 9,081 cases was also identified in 2004, primarily in the southernmost governorates. Four governorates – Dahuk, Basrah, Muthanna, and Thi-Qar – reported this year as their highest incidence.

Iraq also had two major outbreaks of mumps. The first occurred in 2004 and the second one in 2016, with the later outbreak being the larger of the two. In 2004, the governorate of Baghdad saw the most cases of all governorates in that year (3,768 cases). The outbreak spread slightly, with additional cases reported mostly in governorates north of Baghdad. In 2015, the year preceding the second major outbreak, Baghdad governorate saw 10,794 cases and then about four times that number in 2016. The six highest incidences seen among Iraqi governorates between 2001 to 2016 occurred in 2016, while the governorate with the highest incidence in the 2004 outbreak ranked 9th overall among the highest incidences. The outbreak in 2016 also resulted in 13 of the 18 governorates reporting their highest incidence of mumps seen between 2001 and 2016. Among the other governorates, four – Kirkuk, Ninewa, Anbar, and Salah al-Din – reported 2003 or 2004 as the highest incidence, and the highest incidence in Muthanna occurred in 2001.

Lastly, Iraq had one outbreak of rubella in 2004. During this outbreak, Kerbala had the highest incidence of rubella (14.4 per 100,000 persons) and the largest number of cases (113 total). In other years, the governorate of Baghdad often saw the greatest number of cases per year, but, because its population is so large, overall incidence stayed relatively low and was comparable to the other governorates. While several other smaller outbreaks did occur, the disease had limited spread to neighboring governorates, maintaining a relatively stable incidence less than one per 100,000 persons per year, likely due to the low transmissibility of rubella compared to the other infectious diseases we examined.

Vaccine Coverage and Incidence

We identified significant disparity in MMR vaccine coverage. The percent unvaccinated at the governorate level ranged from 0% unvaccinated (Ninewa from 2009 to 2010, Diyala from 2009 to 2011, Najaf in 2008, and Thi-Qar in 2004) to 86% unvaccinated (Anbar in 2007). The largest increase in vaccine coverage, a 57% absolute change, occurred between the years 2008 and 2009 in the governorate of Wassit. The largest decrease in vaccine coverage, a 44% absolute change, occurred between the years 2004 and 2005 in the governorate of Thi-Qar.

The linear-mixed effects model identified a positive significant association between annual measles incidence per 100,000 and MMR vaccine coverage two years prior. For each additional percent unvaccinated, the risk difference in the measles incidence rate was 0.8 cases per 100,000 persons higher, controlling for governorate (p -value < 0.001). However, the governorate-level associations between vaccine coverage and measles incidence differed from the pooled estimates, with four governorates reporting statistically significant increases in measles incidence ranging from 1.614 to 3.732 extra cases per 100,00 persons for each additional percent unvaccinated.

The linear-mixed effects models did not find significant associations between MMR vaccine coverage and incidence of mumps or incidence of rubella. The model suggests mumps incidence decreased with decreasing vaccine coverage and there was almost no difference in rubella incidence as vaccine coverage increased, but neither of these relationships were statistically significant. At the governorate level, there were two governorates with significant associations

between vaccine coverage and incidence for mumps, but these results, -0.153 and 0.432 additional cases per 100,000 persons, contradicted one another in the direction of the association. Meanwhile, three governorates showed positive significant associations between vaccine coverage and incidence of rubella, ranging from 0.014 to 0.182 additional cases per 100,00 persons for each additional percent unvaccinated.

The statistical test we performed measured how many standard deviations above or below the subnational estimates were from the pooled estimate. In the case of measles, the four governorates with statistically significant estimates had larger risk differences than the pooled estimate, and we found more than one standard deviation of separation between them. For mumps, the Z-scores were approximately zero, demonstrating similarity between the pooled and unpooled estimates. For rubella, we saw larger estimates for the statistically significant subnationals than what was seen in the pooled estimate and at least two standard deviations of separation.

Table 1: Relationship between Incidence and Percent of Population Unvaccinated for Measles, Mumps, and Rubella (MMR) in Iraq, 2001-2016

Governorate	Estimate	SE	p-value	Z-score
MEASLES				
<u>Overall</u>	0.818	0.182	< 0.001	
Babylon	3.732	1.159	0.007	-2.484
Baghdad	2.292	0.567	0.002	-2.475
Diyala	1.614	0.434	0.003	-1.691
Qadissiyah	2.141	0.916	0.038	-1.417
MUMPS				
<u>Overall</u>	-0.308	0.231	0.184	
Salah al-Din	0.432	0.192	0.049	-3.201e-4
Sulaymaniyah	-0.153	0.061	0.036	-6.704e-5
RUBELLA				
<u>Overall</u>	0.003	0.005	0.456	
Baghdad	0.014	0.006	0.041	2.177

Erbil	0.182	0.040	0.002	4.589
Najaf	0.014	0.0062	0.034	2.134

Caption to Table 1: MMR data obtained from Iraqi Ministry of Health surveillance reports, 2001-2016, by governorate. Interpretation: For the governorate named, we estimate the number of additional (or fewer) disease incident cases per 100,000 persons for each additional percent unvaccinated.

Interaction with Migration and Vulnerability

Between 2001 and 2007, the total population in each governorate remained relatively consistent with the annual increase fluctuating between 2.5% and 3.3% during these years, likely attributable to general population growth.¹⁵ The only governorate to stand out from this pattern, Salah al-Din in central Iraq, saw decreases in population of 1.3% from 2005 to 2006 and 21.4% from 2006 to 2007, following a mosque-bombing and subsequent violence in the city of Samarra.¹⁶

The first major governorate-level population shift in the post-invasion era occurred between 2007 and 2008, when 14 out of the 18 governorates experienced greater than a 5% increase or 5% decrease in population. During this time, it appears that many Iraqis moved from Diyala and Sulaymaniyah in northeastern Iraq towards the neighboring governorates of Erbil, Kirkuk, and Salah al-Din to the west. UNHCR identified between 40,000 to 50,000 persons of concern in Iraq for each year between 2005 to 2008, but this number spiked to more than 575,000 in 2009. From 2009 to 2010, we observed a reversal compared to 2007 and 2008 when 12 governorates experienced a population change in the opposite direction.

Large-scale displacement and migration continued between 2010 and 2011. Sixteen governorates experienced either increases or decreases in population in the same direction compared to 2007 to 2008. Interestingly, the six governorates with the greatest percent increases in population between 2009 and 2010 had the greatest percent decreases between 2010 and 2011. In 2010, displacement increased with greater than 1.5 million persons of concern throughout the country. At that time, the governorate of Baghdad had the single largest year total with reportedly 428,647 persons of concern residing there. Two other governorates hosted at least 100,000

persons of concern in 2010, Ninewa and Diyala. While displacement dropped in 2011, there were more than 850,000 persons of concern across Iraq in 2012.

After these large redistributions of the population during the peak of the war, governorates returned to their pre-2007 patterns, with almost all governorates experiencing a 2 to 3% increase in population per year. The only outlier was the governorate of Najaf where population increased by more than 11% from 2014 to 2015, balanced by a greater than 5% decrease in population between 2015 to 2016. From 2014 to 2016, governorates in the Kurdistan region hosted the most persons of concern.

Our regression analysis identified a significant relationship between persons of concern and MMR vaccine coverage for measles. For every additional 10,000 persons of concern within a governorate, measles incidence was 0.26 cases per 100,000 higher given constant vaccine coverage (p-value < 0.001). For mumps, incidence was 0.02 cases per 100,000 higher for every additional 10,000 persons of concern within a governorate, but this value was not statistically significant. There was no relationship between the number of persons of concern in a governorate and MMR vaccine coverage for rubella.

Discussion

Between 2007 and 2011, most governorates experienced major shifts in population, as Iraqis became internally displaced within their home governorate or another governorate and Syrian refugees entered the country to avoid the conflict in Syria. Many relocated due to threats, lack of security, and fear of violence, and returning was not usually an option without restoration of food, water, healthcare, and other services.¹⁷ This created pockets of individuals vulnerable to vaccine-preventable diseases within governorates.

Several vaccination campaigns reinforced the resilience of communities. These campaigns protected vulnerable populations against measles, mumps, and rubella and prevented additional transmission when nearby individuals did become infected. Some of the major post-invasion campaigns took place across Iraq in 2003 and 2007.^{4,18} Other campaigns in 2008 and 2009 targeted specific areas to limit the spread of current outbreaks.^{14,19,20} These campaigns improved

levels of coverage and herd immunity which helped prevent outbreaks and protect unvaccinated Iraqis.

Lafta and Hussain's analysis reported an average measles incidence of 2.6 per 100,000 persons when excluding the outbreak years of 2004, 2008-2009, and 2014 and an incidence of 95.7 per 100,000 in 2009.⁷ However, this national incidence number masked the significant geographic disparity in incidence among the governorates. We identified large ranges in incidence of measles, mumps, and rubella, specifically during the outbreak years.

Our analysis of incidence at the subnational level revealed disproportionately higher numbers of cases and subsequent outbreaks in some areas. The heterogeneity in our statistical results demonstrates the complexity of the relationship between vaccine coverage and disease incidence. This variation was further identified by the Z-scores which showed how certain governorates had estimates greater than one or two standard deviations above or below the pooled estimate. It is likely that the interaction of several covariates, beyond what is included in our analysis, play into whether an outbreak occurs.

We further recognized this complexity when we saw positive significant associations between vaccine coverage and disease incidence, both with and without the persons of concern interaction term for measles; similar relationships were not seen for mumps or rubella, however. This does not mean these relationships do not exist, but there are likely many additional factors that contribute to the spread of these diseases and ultimately determine the size of an outbreak. Additional factors include, but are not limited to, environmental-related factors like migration, population density, and access to care, as well as disease-related factors like transmissibility, length of infectious period, and number of contacts.

Demonstrating how conflict undermines a country's health care system can provide evidence to build commitment to reduce conflict and ensure proactive response when it does occur. For the years 2001 to 2016 in Iraq, we did not identify a singular factor that predicted outbreaks of infectious disease. This is important to consider for public health planning because multiple factors, beyond just vaccine coverage and persons of concern, must be addressed to fully limit

disease spread. Well-functioning health systems and targeted interventions programs are necessary to protect vulnerable individuals from preventable infectious diseases.

Limitations

The governorate-level case counts for measles, mumps, and rubella in the dataset likely are underestimates, and the amount of bias varies by governorate. In areas of conflict, it is very likely a considerable number of Iraqis who contracted an infectious disease were unable to access medical services. Since primary health centers are responsible for reporting the number of cases of notifiable diseases they diagnose, missing cases results in underreporting. Also, health centers in the private sector do not report cases to the Iraq MoH whose dataset we used. However, only a few cases likely were missed for this reason because private hospitals focus more on surgery and deliveries than on general hospital care.²¹

Governorate-level incidence per 100,000 persons values are likely underestimates if the health care system missed cases. It is important to consider a potential for collinearity between high conflict and low case reporting that may also be associated with low or declining vaccine coverage.

Missing data was also a problem for several governorate-years. Primarily, data was missing from the Kurdistan Region of Iraq which is made up of Iraq's three northernmost governorates of Erbil, Dahuk, and Sulaymaniyah. The autonomous region now also includes Halabja Governorate which split off from Sulaymaniyah in 2014, but the dataset did not specifically represent this new governorate.²²

Conclusion

The Iraq War undermined the nation's health system, generating large fluctuations in vaccine coverage. Humanitarian groups, in combination with the Iraqi Ministry of Health, worked to supplement health care by organizing successful vaccination campaigns aimed at preventing the spread of infectious disease outbreaks and repairing components of the cold chain. We identified a significant association between higher MMR vaccine coverage and lower measles incidence between 2001 and 2016 in a pooled subnational estimate, controlled for governorate, and an

increase in incidence for larger numbers of persons of concern. However, the pooled estimates for mumps and rubella did not show these same associations, and only some governorates in our unpooled analysis had statistically significant relationships for each infectious disease.

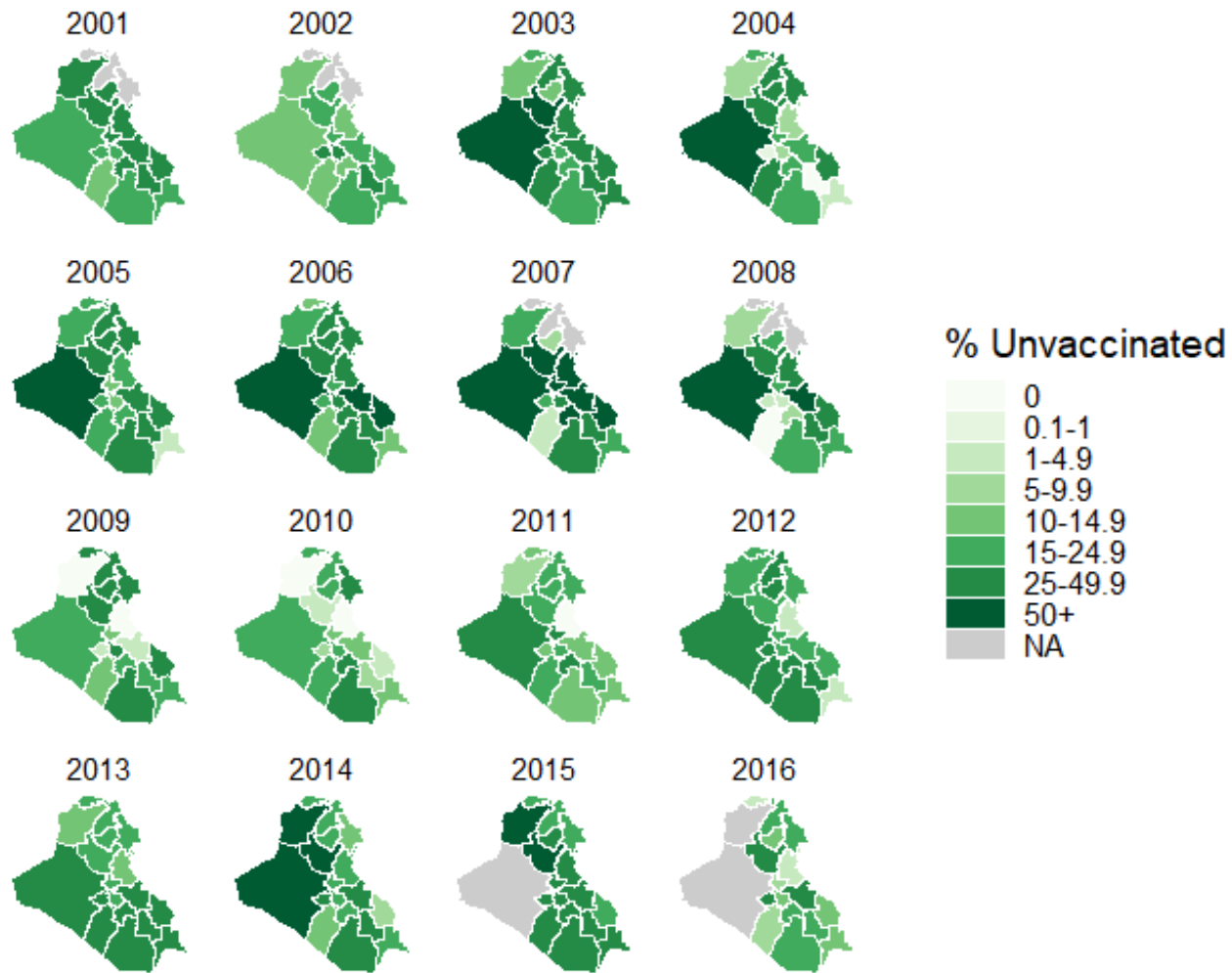
Therefore, the variables we chose to examine are likely only a few of a combination factors that interact to determine whether an outbreak occurs.

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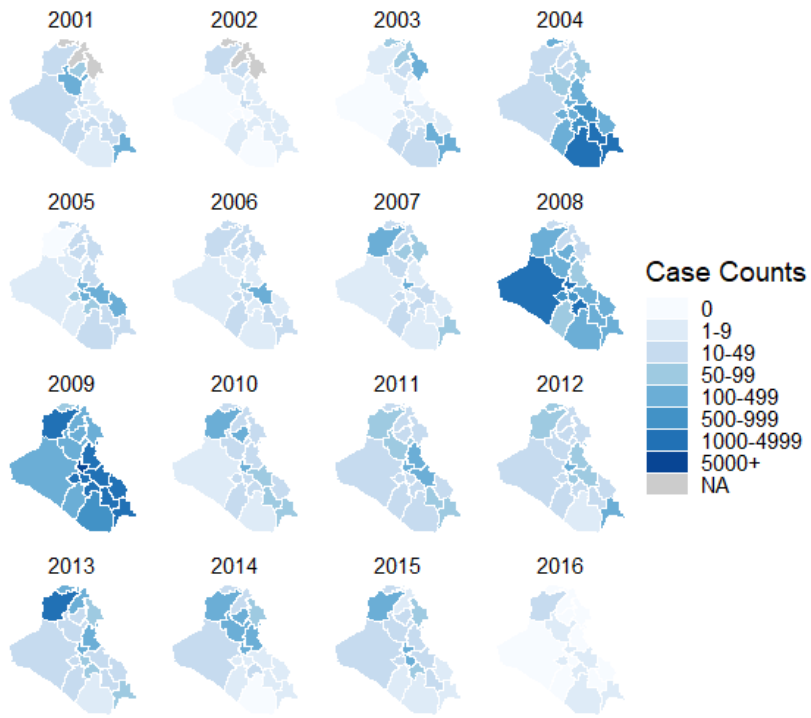
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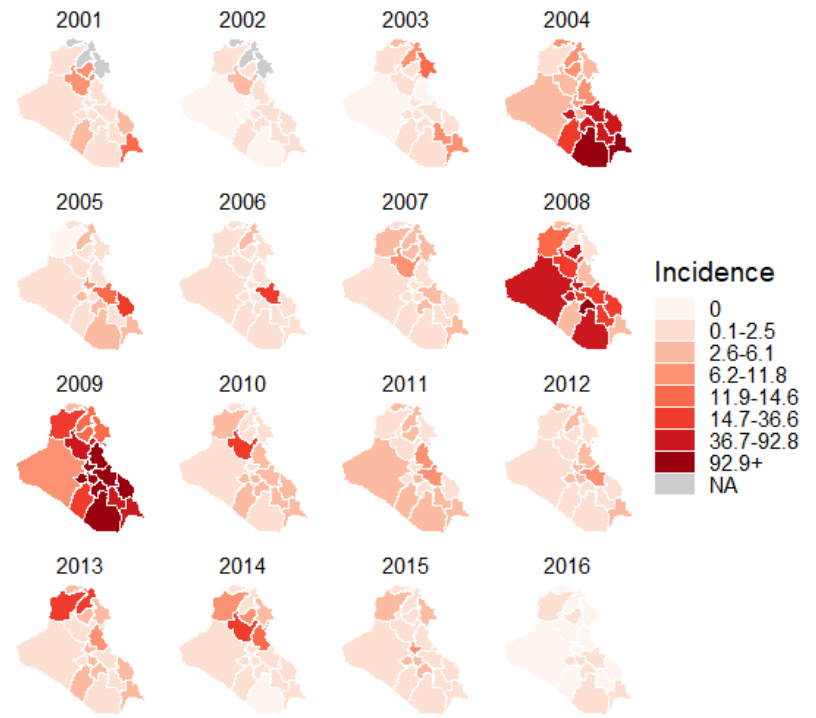
Appendix A



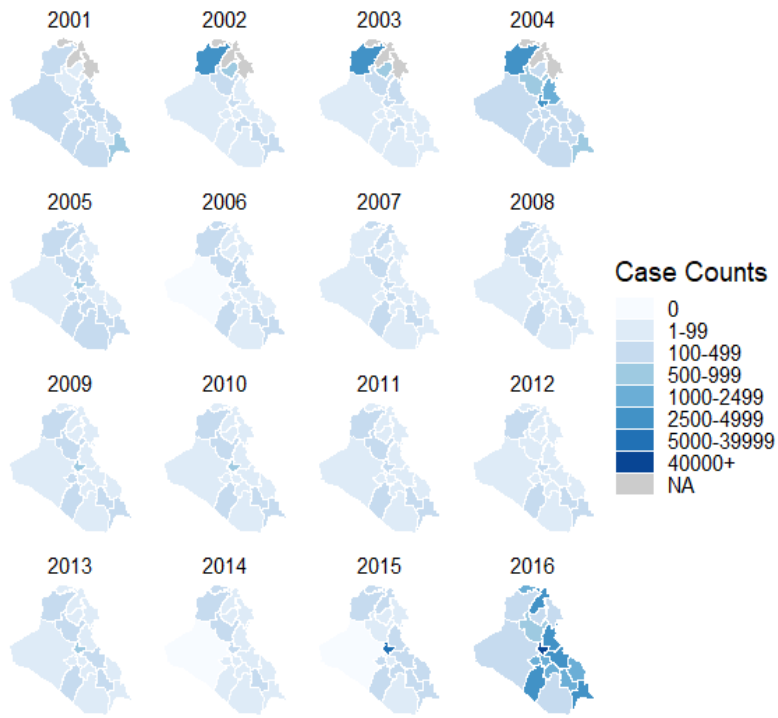
MMR Coverage in Iraq, 2001-2016



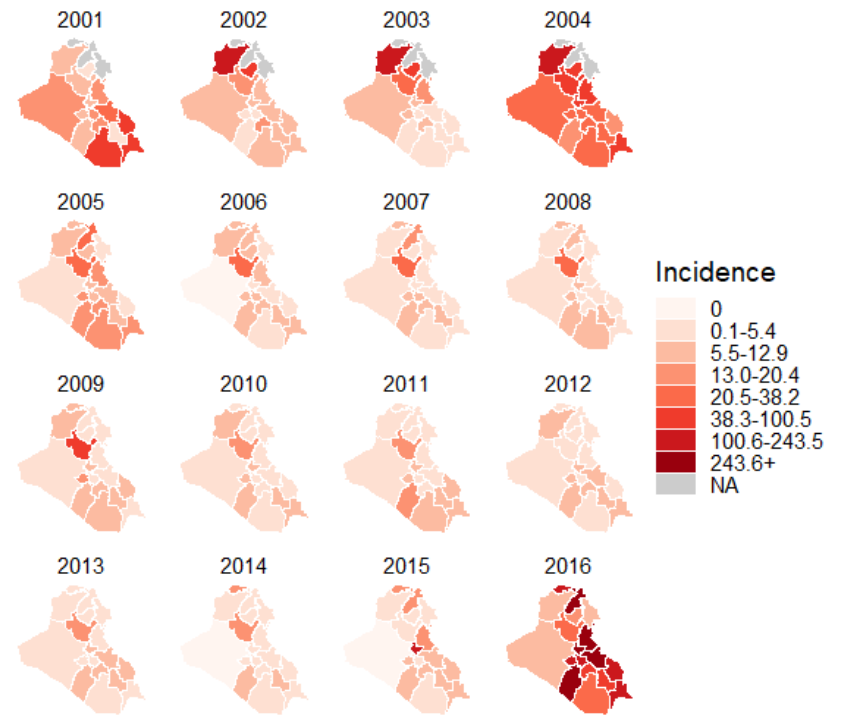
Measles Cases in Iraq, 2001-2016



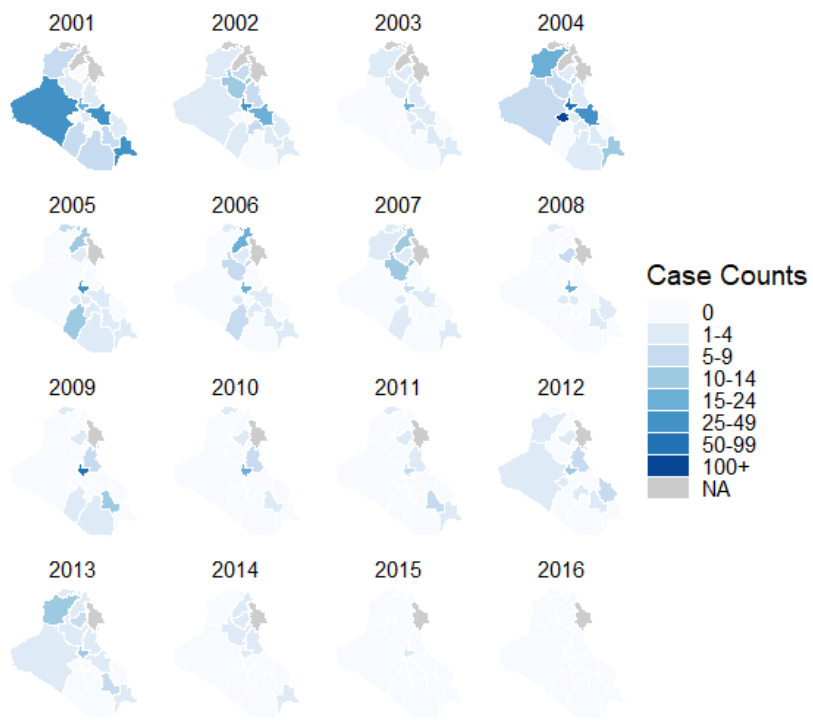
Measles Incidence in Iraq, 2001-2016



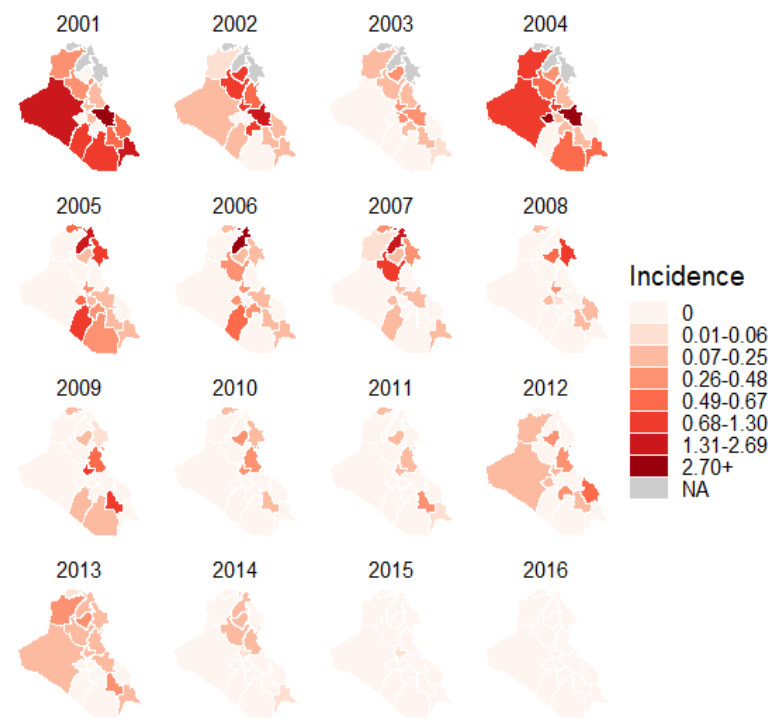
Mumps Cases in Iraq, 2001-2016



Mumps Incidence in Iraq, 2001-2016



Rubella Cases in Iraq, 2001-2016



Rubella Incidence in Iraq, 2001-2016

Appendix B

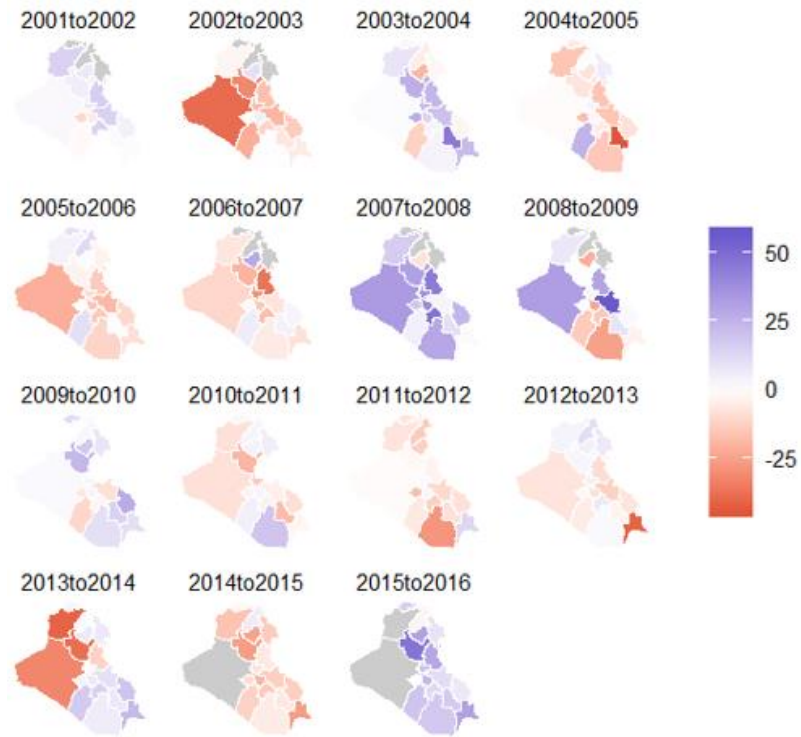


Figure 1: Absolute Change in MMR Vaccine Coverage from Previous Year

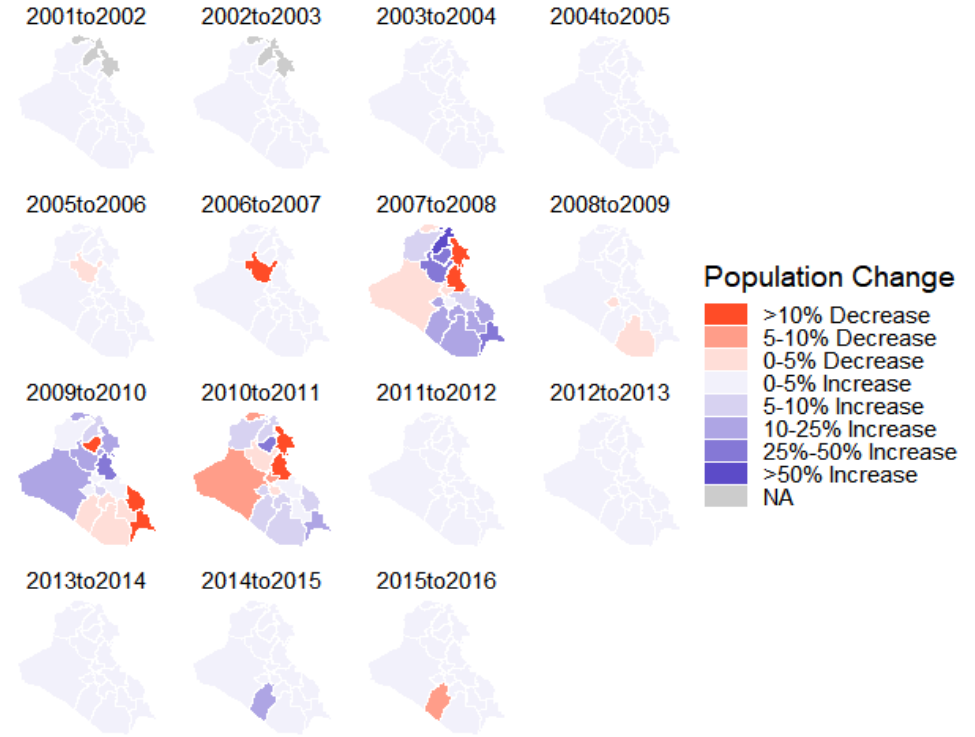


Figure 2: Percent Change in Population from Previous Year

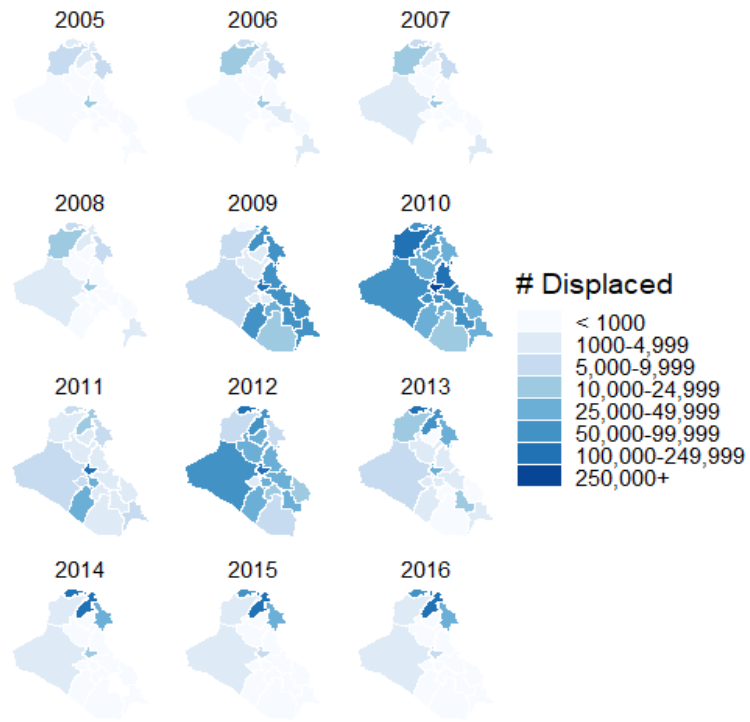


Figure 3: Total # of Persons of Concern by Governorate