Descriptive Finding

Influenza mortality in French regions after the Hong Kong flu pandemic

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# Contents

1 Introduction 546

2 Methods 548
2.1 Data 548
2.2 Statistical analysis 549

3 Results 550

4 Discussion 554
   References 558
   Appendix 564
Influenza mortality in French regions after the Hong Kong flu pandemic

Florian Bonnet¹
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Abstract

BACKGROUND
Influenza mortality has dramatically decreased in France since the 1950s. Annual death rates peaked during two pandemics: the Asian flu (1956–1957) and the Hong Kong flu (1969–1970).

OBJECTIVE
This study’s objective is to evaluate whether the second pandemic created a structural change in the dynamics of influenza mortality in France.

METHODS
We employ a new database on influenza mortality since 1950 at the subnational level (90 geographic areas) to estimate statistical models to find out whether a structural change happened and to explain the differences in mortality rates across geographic areas. Influenza mortality increased between 1950 and 1969 and decreased from 1970 onward.

CONCLUSIONS
The Hong Kong flu is identified as the event of a structural break. After the break, geographical differences are less explained by regional characteristics such as income, density, or aging ratio. The Hong Kong flu was found to be associated with a major change in influenza mortality in France. Change in health practices and policies induced a decline in mortality that started in 1970, just after the pandemic. The health benefits are notably important for senior citizens and for the poorest regions.

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1. Introduction

The COVID-19 pandemic has strongly afflicted France, yet little attention has been given to health outcomes following previous pandemics. Pandemics are dramatic shocks. They have the ability to positively transform health systems and practices over the long run as they generate political and economic support for medical innovation and health care improvement (Dehner 2010; Morens, Taubenberger, and Fauci 2009; Jordà, Singh, and Taylor 2020; Iskander et al. 2013). Before COVID-19, and aside from the global HIV epidemic, only two pandemics severely affected France after WWII: the Asian flu (1956–1957) and the Hong Kong flu (1969–1970). Death tolls of these pandemics were much lower than that of the current crisis, even adjusted for population and age distribution changes: 33,232 deaths from the Asian flu and 32,062 deaths from the Hong Kong flu. The main difference is that in earlier pandemics, the mortality rates of infants and young adults were higher than those of today.

In the aftermath of these two pandemics, international health authorities and industrialized countries carefully crafted responses, shared information, established surveillance, strengthened vaccine studies, and implemented vaccination campaigns against influenza (Tyrrell et al. 1970; Carrat and Valleron 1995; Sands, Mundaca-Shah, and Dzau 2016; Viboud et al. 2005; Aranzazu 2013; Vagneron 2015). The aim of our study is to evaluate whether this was effective and, more precisely, whether these pandemics created a structural break in the trend line of France’s flu mortality. To do so, we examine a unique historical database that tracks flu mortality by region. Our contribution is threefold. First, we provide a refined description of influenza pandemics and seasonal influenza in 90 French geographical units from 1950 to 2015. Second, we establish that winter 1969–1970 does indeed represent a structural break in the spread and control of seasonal and pandemic influenza in France, especially for the elderly, confirming a major turning point in France’s flu management. Third, we show that after 1970, influenza mortality became regionally random, no longer dependent on income, density, and the share of elderly people.

The Hong Kong flu led to a sharp increase in the flu death rate: In 1969 it was 30 per 100,000 in France, compared to an average of 14 per 100,000 between 1965 and 1974. Moreover, Figure 1 reveals that geographic variations were significant: Death rates were lower in the north of France (with a minimum of 12.5 per 100,000 in Seine) and higher in the southwest (with a maximum of 76.4 per 100,000 in Creuse). Despite a multilevel response to the Hong Kong flu aimed at preventing future such health shocks, the current crisis reveals that France was not fully prepared. However, we show that pandemics can change health practices for the better, as the Hong Kong flu episode is found to be associated with a reduction in both mortality and inequalities therein across regions.
Figure 1: Map of flu death rates by department in 1969 (deaths per 100,000 population)
2. Methods

2.1 Data

We gathered original death data by cause, geographical unit (département in French; hereafter department), and sex for the period 1950–2015. The data were retrieved from Statistique des Causes de Décès, published by Institut National des Statistiques et des Etudes Economiques (INSEE) for the period 1950–1978, and from Institut National de la Santé et de la Recherche Médicale (INSERM) for the period 1979–2015. Figures come from the International Classification of Diseases short list. Official statistics follow the classification of the sixth revision from 1950 to 1957, the seventh revision from 1958 to 1967, the eighth revision from 1968 to 1978, the ninth revision from 1979 to 1999, and the tenth revision from 2000 to 2015. We retrieved deaths due to influenza as well as total deaths by department and sex for the entire period.

Our study focuses on mainland France and does not include overseas territories. We use the classification of the 90 departments that prevailed before 1968, but we also provide analysis by aggregating the data into 22 geographical regions.

For the statistical analysis, we also use population data by department, sex, and age at January 1. These populations are calculated from age-specific populations in census years and annual vital statistics (age-specific deaths and births) using a methodological protocol close to that of the Human Mortality Database (Bonnet 2020; Barbieri et al. 2015). To determine the population on January 1 of years in an intercensal period, we adjust the population at the initial census by both observed deaths and by an estimate of migration flow since the initial census. The overall intercensal migration flow is estimated by comparing the observed population and the theoretical population at the final census. The theoretical population is equal to the initial census population minus observed deaths during the intercensal period. The intercensal migration flow is then distributed temporally in proportion to the time elapsed since the initial census. To compute death rates in year t, we use the mean of population at January 1 of year t and t+1.

We also use income data by department (Bonnet and Sotura 2021; Bonnet, d’Albis, and Sotura 2021). Incomes are calculated using tax tabulations for the periods 1960–1969 and 1986–2015 and aggregate income tax statistics for the periods 1922–1959 and 1970–1985. This income includes public transfers related to the pension system but does not take into account taxes due or public subsidies provided to households.
2.2 Statistical analysis

We aim to identify whether and when there was a structural break in the control of influenza epidemics in France. We use a Poisson model, which prevents negative values for death rates, and regress deaths on a continuous year variable, a post-year dummy, and the interaction of a post-x-year dummy, in addition to department-specific time trends, department fixed effects, and specific controls (population density per square kilometer, per-capita income in 2015 euros, and the share of people aged 65 and older in the population). To take into account the difference in department sizes, we use population as an offset in this regression. We repeat the procedure, allowing the post-year dummy to vary from 1960 to 1980. The year with maximum in log-likelihood is considered to be the year of a structural break in the data. This test is similar to the Quandt likelihood ratio test, which has been shown to be a reliable test for structural breaks in cases of unknown break points (Quandt 1960; Andrews 1993; Piehl et al. 2003).

We also perform a spatial analysis. We examine the differences in deaths across departments using a Poisson model and three specific variables: population density per square kilometer ($D$), income per capita in 2015 euros ($Inc$), and the share of people aged 65 and older in the population ($Sh_{d}^{65+}$). For each year of the period 1950–2015, we estimate the coefficients of the following equation:

$$\log(m_{d}^{Flu}) = \alpha + \beta_1 D_d + \beta_2 I_d + \beta_3 Sh_{d}^{65+} + \varepsilon_d, \quad (1)$$

where $d$ is the department and $\varepsilon_d$ is the difference between observed and estimated mortality due to flu. If positive, the difference is defined as excess mortality. To compute confidence intervals around our estimates, we consider over-dispersion in the model. Finally, we compute pseudo $R^2$ of our model for each year as the square of the correlation between estimated and observed departmental values. All our computations are done using R. software. Table 1 presents descriptive statistics for variables used in Equation (1) and specific years.
Table 1: Descriptive statistics

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<tr>
<td>Flu death rate</td>
<td>5.25</td>
<td>32.03</td>
<td>18.1</td>
<td>2.41</td>
<td>5.69</td>
<td>3.45</td>
<td>0.24</td>
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<td>(2.98)</td>
<td>(11.96)</td>
<td>(8.67)</td>
<td>(1.67)</td>
<td>(4.84)</td>
<td>(2.17)</td>
<td>(0.27)</td>
<td></td>
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<tr>
<td>Density</td>
<td>183.21</td>
<td>205.11</td>
<td>233.26</td>
<td>234.86</td>
<td>239.67</td>
<td>245.53</td>
<td>263.25</td>
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<td>(1069.73)</td>
<td>(1209.71)</td>
<td>(1394.3)</td>
<td>(1342.6)</td>
<td>(1334.17)</td>
<td>(1349.34)</td>
<td>(1452.56)</td>
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<tr>
<td>Income per adult</td>
<td>2407.63</td>
<td>3855.42</td>
<td>6720.35</td>
<td>9896.5</td>
<td>11327</td>
<td>13402.45</td>
<td>15488.09</td>
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<tr>
<td>(615.77)</td>
<td>(788.22)</td>
<td>(1153.78)</td>
<td>(1328.44)</td>
<td>(1415.24)</td>
<td>(1487.54)</td>
<td>(1465.79)</td>
<td></td>
</tr>
<tr>
<td>Share of 65+</td>
<td>12.46</td>
<td>12.56</td>
<td>13.94</td>
<td>15.6</td>
<td>15.66</td>
<td>18.07</td>
<td>19.03</td>
</tr>
<tr>
<td>(2.07)</td>
<td>(2.09)</td>
<td>(2.53)</td>
<td>(3.15)</td>
<td>(3.2)</td>
<td>(3.44)</td>
<td>(3.24)</td>
<td></td>
</tr>
</tbody>
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Notes: We provide mean and standard deviation (in parenthesis) for 90 departmental values. Flu death rates are per 100,000. Income per capita is in 2015 euros.

3. Results

The test for a trend break in mortality between 1950 and 2015 identifies 1968 as the year with the maximum in log-likelihood. Values are roughly similar for each year of the period 1968–1971 and highly decrease in 1972. There are other spikes related to influenza outbreaks (1974 and 1977), but they are smaller in magnitude. We note that sensitivity testing of our regression does not affect our main conclusions. We retain 1970 as the year of the structural break for our subsequent analyses since it is the end of the Hong Kong flu and the central year of the period 1968–1971.

We present a range of graphs to illustrate our empirical results. Figure 2 shows flu mortality by region from 1950 to 2015. The red lines provide estimates of mortality trends for the periods 1950–1970 and 1970–2015 using a Poisson model. The Hong Kong flu period (1968–1970) appears in gray. The last figure provides flu-specific mortality at the national level while Figures A-1, A-2, and A-3 in the appendix provide flu mortality by department. In France we find a sharp decline in flu mortality between 1950–1960 and 2005–2015, of a magnitude between 84% and 98%. This decrease is sustained over time and converges toward 5 per 100,000 on average in 2015. Importantly, we observe that before 1970, almost no region or department exhibits a negatively sloped mortality trend. Mortality was in fact increasing before the Hong Kong flu and decreased thereafter.
Figure 2: Flu death rates by region (deaths per 100,000 population)


Figure 3 plots mean flu death rates in France’s 90 departments between 1950 and 1968 against the variation in mean flu death rates between 1950–1968 and 1970–2015. The slope of the relationship is −0.64. This reveals a strong convergence across geographical units; in addition to across-the-board declines in flu-specific mortality, the initially high-mortality departments essentially caught up to the initially low-mortality departments. This convergence is associated with a reduction in geographical inequalities, as documented for the general mortality (Bonnet and d’Albis 2020).
Figure 3: Declines in flu-specific mortality across departments (deaths per 100,000 population)

Notes: This figure plots mean flu death rates between 1950 and 1968 and the variation in mean flu death rates between 1950–1968 and 1970–2015 for France’s 90 departments. The result of the regression is plotted in red. The value of the slope is equal to −0.65.

Figure 4 provides a decomposition by age group of flu-specific mortality in France. These results suggest that the break caused by the Hong Kong flu affected only adults, particularly senior citizens. The decline in flu mortality for those under age 25 started much earlier, and 1970 death rates for those aged 1 to 44 were already very low. Thus the shock of the Hong Kong flu appears to have induced the health care system to devote more attention to flu mortality among the elderly. The death rate of those 65 and up shifted from an average of 200 deaths per 100,000 in the 1960s to an average of 30 per 100,000 in the 1980s. The response to the COVID-19 crisis echoes such consideration, initiating a historic worldwide effort to predominantly protect the elderly. We also notice that the structural break holds for both men and women, with the death rate of the latter being slightly higher due to differences in age structure.
Figure 4: Flu death rates by age group and sex in France (deaths per 100,000 population)


Figure 5 plots the coefficients estimated in the linear regression characterizing geographical death rates over time. Notably, it reveals that per-capita income explained flu mortality rates in some major flu outbreaks prior to and during the Hong Kong flu: Controlling for population density and the share of people aged 65 and up, those with higher incomes had lower mortality rates. This disadvantage for the poorest departments was reduced after the Hong Kong flu. Thus improved health practices benefited the poorest departments, which had suffered more than others from the flu. Overall, we note that after the Hong Kong flu, differences in these characteristics explain decreasing amounts of variation in geographical differences in flu mortality: the pseudo $R^2$ associated with each annual regression decreases to close to 0 in 2010 after reaching its maximum (0.52) in 1969. We interpret this as flu mortality becoming more regionally stochastic.
4. Discussion

The Hong Kong flu pandemic started in July 1968 and lasted until 1970. Despite the staggering death toll, the Hong Kong flu pandemic and its repercussions are surprisingly poorly documented in France (Flahault and Zylberman 2010). Beyond natural immunity, whose role is difficult to assess in the medium run (Jackson, Vynnycky, and Mangtani 2010), what could be behind such a strong decline in influenza across all departments in France after 1970? It is difficult to identify any major progress in hygiene at that time (Flahault and Zylberman 2010). The introduction of single-use handkerchiefs dates to the 1930s, and massive use of hydro-alcoholic gel dates much later. Surveillance has indeed been improved, but this progress seems to have taken place mainly during the 1980s. Finally, there is also little chance that France’s influenza is strongly correlated with economic growth or crises (Ruhm 2000; Brüning and Thuilliez 2019).
As we examine what caused the decline, the distinction between pandemic and seasonal flu is important (Brüning and Thuilliez 2019). France has not experienced a severe pandemic since 1969, either because the world has been better prepared or just because of chance. Put differently, reduced seasonal flu mortality after 1970 may not have been influenced by pandemics but rather may be part of a pattern of seasonal flu (Carrat and Valleron 1995; Rizzo et al. 2007; Guérin 2007; Gottfredsson et al. 2008; Valleron et al. 2010; Hannoun 2013; Brès 1980). Figure A-4 and A-5 in the appendix hence test for the sensitivity of our results to the presence of pandemics and provide the change in slope when we exclude the 1957 and 1968 pandemics, assuming a value for these particular years as equivalent to the average mortality before 1970. The difference between the slopes gives us the contribution of pandemics to the average mortality trend. When both pandemics are eliminated, the slopes before 1970 (in blue) move downward for all regions and age groups and mostly for those age groups most affected by pandemics, but the structural break remains apparent. This confirms the influence of pandemics in the change in flu mortality.

A change in vaccination practices could be among the most plausible explanations for the structural break (Meslé 2010). Lacking historical data, we were unable to find reliable figures on the production of influenza vaccines in France from 1950 to 1976. However, the WHO delivered vaccination recommendations in the early 1970s; various public health organizations were also founded at that time (Brès 1980). Figure A-6 in the appendix provides tentative estimates of influenza vaccination in France from 1950 to 2015 from unpublished data, and they indicate an increase after 1970. We do not have data on vaccination at the subnational level by age group or socioeconomic status over this period, to the best of our knowledge. The vaccination rate before 1977 is therefore estimated according to four scenarios because we do not have data for this period in France. However, influenza vaccination principles were already well-known at that time, and the population had been aware of vaccination benefits since the Pasteurian revolution.

Figure A-7 in the appendix illustrates that the epidemic was well covered by the media (MacCarthy 1969), as exemplified by an interview with Robert Boulin, the health minister, who got vaccinated and strongly recommended it to the population. Another article documents the high demand for vaccines faced by pharmacies. In addition, Figure A-8 in the appendix shows that flu-specific mortality for senior citizens is highly correlated with vaccination in the recent period, as we observe a decline in vaccination, notably during the 2009 A(H1N1) influenza pandemic (Vaux et al. 2011; Blondel et al. 2012; Peretti-Watel et al. 2013) and an increase in mortality since 2010. Other technological and medical advances, some related to comorbidities or complications of influenza, may also have played a role. Pneumococcal vaccines, for example, help reduce influenza mortality (Fedson 1998). Nevertheless, in France, whether the public is willing...
to accept vaccination when it is available remains important (Schwarzinger et al. 2010; Peretti-Watel et al. 2020).

Studies on this topic may also include pneumonia deaths. The counterpart of Figure 2 for pneumonia-related death is provided in Figures A-9a and A-9b in the appendix. The patterns are quite different for that of influenza. Interestingly, we observe a hump in the 1990s, certainly due to the HIV-AIDS epidemic. The decline also coincides with the introduction of highly active antiretroviral therapies (McCullers 2013; Metersky et al. 2012; Shrestha et al. 2015). Post-influenza bacterial pneumonia is a major cause of morbidity and mortality associated with both seasonal and pandemic influenza virus illnesses. However, understanding the role that influenza plays on the population-level epidemiology of bacterial pneumonia and, reciprocally, the role of bacterial pneumonia in complicating influenza remains a challenge, which is why we prefer to keep both causes of death separated (Feikin et al. 2004; Franquet and Domingo 2022; Roux et al. 2014). We also replicate Figure 2 for all-cause mortality in Figure A-10 in the appendix. There is no break in this period, which reinforces our argument about a specificity of the flu.

A “dry tinder” effect may mitigate our story on structural changes in the short run (Rizzi, Søgaard, and Vaupel 2021). Indeed, harvesting could partly explain the fall in mortality and also the decline in the role of income after 1970. The dry tinder effect has been well documented by epidemiologists; it is a situation in which a soft year creates a larger group of susceptible individuals the following year. We recognize that such a selection effect could partly explain the fall in mortality in the short run. However, after a few years, the most vulnerable age groups (infants and elderly) are replaced by new cohorts, and the effect is less likely to explain the change we observe. Moreover, Figure A-6 in the appendix shows that vaccine uptake increases substantially after 1969.

We also use our model over the entire period (rather than year by year) to predict values at the national level. The difference between the observed values and the predicted values is excess deaths. We report this in Figure A-11 in the appendix. We can see clearly two periods: before and after the Hong Kong flu. Years of excess deaths are associated with the main epidemics, and from the 1970s onward, we observe a permanent under-mortality. The 2009 H1N1 pandemic had relatively low mortality effects in France. However, it is true that the 2009 H1N1 pandemic changed public attitudes toward vaccination in France (Lemaitre and Carrat 2010; Lemaitre et al. 2012; Boëlle et al. 2020; Fuhrman et al. 2010). We note that in mainland France, the 2010–2011 season was characterized by an influenza epidemic of moderate intensity, which occurred between late December 2010 and mid-February 2011. Severe cases admitted to the ICU had epidemiological characteristics and lethality comparable to those observed during the 2009–2010 pandemic, and vaccine hesitancy increased in France after the H1N1 pandemic (Schwarzinger et al. 2010; Ward et al. 2019; Belchior et al. 2011).
Lastly, this paper has some limitations. First, Figure 2 shows subnational heterogeneity of levels and trends. When pooling all regions, we obtain a break in 1968, and when we separate our dataset by region, we obtain 1968 or 1969 as a break in 18 regions out of 22 (two for 1970, one for 1967, one for 1974). Therefore, overall, our results seem to be consistent across regions despite different magnitudes in the breaks observed at the regional level. They mostly confirm that the break is at least in 1968 and not before this date, except for one region. Disaggregating even more at the department level may of course lead to more heterogeneity. Second, we use crude death rates in this paper. Crude death rates describe how many people die out of a given population over a specific time period but take no account of the population’s age distribution when age-standardized measurements of mortality are not available. We use as a control in each model the share of the population aged 65 and over, ages at which influenza mortality is highest. We could control for the share of each five-year age group. Because we stratify the data and present the results without aggregating the stratum-specific information over the strata, we prefer to use crude death rates. Third, our graphical results and regression methods are not fully causal, but our approach and our robustness tests concerning the date of the break are suggestive of a causal explanation.

In conclusion, we found the Hong Kong flu to be associated with a major change in influenza mortality in France. Using a unique dataset of 90 geographical units since 1950, we found a decline in mortality beginning in 1970, just after the major pandemics. The change was most notable for senior citizens and the poorest regions. These facts are useful for putting the recent COVID-19 crisis in perspective. First, they reveal that health behaviors and policies are impacted by these dramatic events (Morse 2007); we can thus expect profound changes to our health system in the coming years. Second, they suggest that the value of elderly life became more important in the late 1960s, a paradox for a period that is usually perceived as a golden age for youth. Finally, the flu’s geographical differences were strongly reduced after the 1970s, with mortality rates that became less correlated to regional mean income. Geographical prevalence becomes a random event, and pandemics may thus hit regions differently, as we have seen in the COVID-19 crisis. The COVID-19 pandemic is thus a good example indicating that preparedness and former pandemic experience played a key role in crisis management. However, better preparedness cannot hinder the probability of pandemics occurring, all the more if the disease was not circulating before its sudden emergence.
References


Bonnet, d'Albis & Thuilliez: Influenza mortality in French regions after the Hong Kong flu pandemic


Appendix

Figure A-1: Flu death rates by department, Ain to Gard (deaths per 100,000 population)

Figure A-2: Flu death rates by department, Haute-Garonne to Oise (deaths per 100,000 population)

Figure A-3: Flu death rates by department, Orne to Territoire de Belfort (deaths per 100,000 population)

Figure A-4: Flu death rates by region, with and without 1957 and 1968–1969 pandemics (deaths per 100,000 population)

Figure A-5: Flu death rates by age group, with and without 1957 and 1968–1969 pandemics

Figure A-6: Flu death rate and vaccination in France from 1950 to 2015 (deaths per 100,000 population)

Notes: This figure plots the flu death rate (in black) as well as vaccination rates (in red and green) by year for the period 1950–2015. The vaccination rate before 1977 is estimated according to four scenarios: a linear trend (green line) and three exponential trends (in red), with vaccination rates equal to 10%, 5%, and 2% in 1970. The Hong Kong flu (1968–1970) is shown in gray. The vaccination rate from 1977 onward comes from http://www.infectiologie.com/UserFiles/File/medias/enseignement/du-lyon/2014-DUCIV-Lyon-Escuret_vaccin_grippe.pdf (page 79) and http://www.grippe-geig.com/couverture-vaccinale.html.
Figure A-7: Evidence from newspapers: France Soir, Paris Presse, and L’intransigeant (December 5, 1969; December 14, 1969; January 7, 1970)
Figure A-8: Flu death rates (in log) for older age groups in France, 1980–2015

Notes: This figure reproduces Figure A-3 and zooms on the period 1980–2015 for those aged 65 and older.
Bonnet, d’Albis & Thuilliez: Influenza mortality in French regions after the Hong Kong flu pandemic

Figure A-9a: Pneumonia death rates by region (deaths per 100,000 population)

Figure A-9b: Pneumonia death rates by age (deaths per 100,000 population)

Figure A-10: All-cause death rates by region (deaths per 100,000 population)

Notes: This figure plots excess deaths caused by flu. We estimate the model presented in Equation (1) over the entire period rather than year by year and define excess deaths as the difference between estimated and observed deaths caused by flu.
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