Short Report

Long-run effects of early childhood exposure to cholera on final height: Evidence from industrializing Japan

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ABSTRACT

Pandemic cholera is one of the most topical and urgent issues in many developing countries. However, although a growing body of research has shown the negative long-run effects of infectious disease exposure on human health, the long-run influences of early childhood exposure to cholera have thus far been understudied. To bridge this gap in the body of knowledge, we draw both on new data describing adult height from 1899 to 1910 from comprehensive official Japanese army records and on data recording the regional variation in the intensity of cholera pandemics. By using a difference-in-differences estimation strategy, we find that exposure to pandemic cholera had stunting effects on the final height of men at that time. Our estimates also suggest that early-infancy exposure to cholera seems to have a stronger long-run effect on adult height than late-infancy exposure.

1. Introduction

One of the most topical and urgent issues in many developing countries is cholera pandemics due to the spread of the Vibrio cholerae bacillus (Harris et al., 2012). The current (seventh) cholera pandemic that started in 1961 has not yet converged and continues to cause a heavy burden worldwide (Hu, Liu, & Feng, 2016). Indeed, recent estimates show 2.9 million that cases of infections and 95,000 deaths occur every year, predominantly in Asia and Africa (Ali, Nelson, Lopez, & Sack, 2015; Didelot, Pang, & Shou, 2015). Although the mechanisms of cholera epidemics have been widely investigated, the persistent effects of pandemic cholera on human health have been understudied (Muteja, Kim, & Thomson, 2011).

The long-run adverse effects of early-life exposure to infectious diseases on health and socioeconomic outcomes have attracted wide attention. A growing body of the literature has examined the impacts of malaria (Barofsky, Anekwe, & Chase, 2015), typhoid fever (Beach, Ferrie, Saavedra, & Troesken, 2016), yellow fever (Saavedra, 2017), and influenza (Ogasawara, 2017). Almond and Currie (2011a) and Currie and Vogl (2013) provide comprehensive reviews of previous studies. As for historical cholera infections, Acemoglu and Johnson (2007) investigate the relationship between predicted mortality from various diseases including cholera and life expectancy. More recently, Ambrus, Field, and Gonzalez (2015) study the persistent effects of the cholera epidemic in 19th-century London on real estate prices. However, despite the frequent outbreak of cholera in the world, little is known about the potential long-run influences of early-life exposure to cholera on human health.

To bridge this gap in the body of knowledge, we estimate the effects of early childhood exposure to cholera on the final height of Japanese men. The strengths of the present study are as follows.

First, we draw on new data describing adult height from 1899 to 1910 by compiling comprehensive official Japanese army records. While previous studies have investigated the association between fetal flu exposure and adult height by using interview survey data (Mazumder et al., 2010), our dataset covers virtually the entire male population at age 20 at that time, which enables us to measure the overall impacts of the cholera epidemic on population health. The panel structure of the data allows us to compare the average height of affected and non-affected cohorts by using the difference-in-differences approach, controlling for a set of unobservable factors, which is difficult for the cross-sectional individual-level datasets often used in previous studies to deal with.

Second, we take advantage of the random variation in cholera epidemics throughout the Japanese archipelago to identify the effects of early-life cholera exposure on height. Since cholera is an acute watery diarrheal disease that leads to severe watery stools and diarrhea, maternal nutritional deprivation can be stronger than in other infectious
diseases (Clemens et al., 2017). This fact implies that infection by the cholera bacterium could impose a heavy burden on the fetus and infants owing to the inadequate nutrition of mothers and infants and could thus be an appropriate exogenous treatment for testing the long-run exposure effects. Another advantage of our analysis is that we use the incidence rate rather than the mortality rate adopted in previous studies (Currie & Vogl, 2013), thereby minimizing the potential measurement error in our key exposure variable.

The present study offers evidence on the long-run adverse effects of early-life cholera exposure as a case study of industrializing Japan, a past-developing Asian country in which the public health environment was similar to those in current developing countries (Lin & Liu, 2014; Ogasawara, 2017). A growing body of research investigating the impacts of fetal exposure to infectious diseases has focused on developed countries for which detailed individual-level datasets are available (Almond & Currie, 2011a; Currie & Vogl, 2013). However, as for cholera epidemics, both South and East Asia are important pathogenic reservoirs and sources of international transmissions (Didelot et al., 2015). Therefore, the findings of this study could explain the potential long-run health effects of pandemic cholera on people in developing countries today, especially in Asia. Moreover, given the associations between wealth and human physique found in recent works (Bozzoli & Quintana-Domeque, 2014), understanding the impacts of exposure to cholera on physical development is an important research topic, especially for developing economies.

The structure of the remainder of the paper is as follows. Section 2 examines the empirical setting. Section 3 presents the main results. Section 4 discusses the results and concludes.

2. Empirical setting

2.1. Pandemic cholera and possible channels

Cholera was prevalent during the late 19th century in Japan. Having been brought to Japan in September 1877 on a British trading vessel, cholera spread throughout the country with devastating consequences. There were 162,637 infected people and 105,786 deaths in 1879, and 155,923 infected people and 108,405 deaths from cholera in 1886. As illustrated in Fig. 1, which shows the trend in the ratio of cholera infections and deaths, cholera continued to be prevalent until around 1890. The government quickly recognized polluted drinking water as the cause of infections by waterborne diseases, including cholera. Nevertheless, temporary measures were unable to lower the risk of cholera infection, as Fig. 1 shows (see Appendix A.1 for more details).

\[ \text{Height}_{it} = \alpha + \beta \text{Cholera}_{it} + \lambda_i + \nu_i + \epsilon_{it} \]  

(1)

where \( \text{Height}_{it} \) is the mean final height of men in regiment \( i \) of prefecture \( j \) and year \( t \), and \( \text{Cholera}_{it} \) is the cholera incidence rate. We use the cholera incidence rate in the two years before birth to the four years after birth to fully capture the potential negative effects of cholera exposure. \( \lambda_i \) is a vector of the prefecture year-level control variables and \( \nu_i \) is a year fixed effect. Note that several regiments are classified into two prefectures. Thus, we use the regiment prefecture-specific fixed effect (\( \nu_i \)) rather than the simple regiment fixed effect (\( \xi_i \)). \( \epsilon_{it} \) is the regiment prefecture-specific time trend and \( \epsilon_{it} \) is a random error term.

Fig. 1. Cholera pandemics in Japan, 1877–1911. Notes: The incidence rate is the number of cholera patients per 1,000 people. The death rate is the number of deaths from cholera per 1,000 people. Sources: See Appendix B.2.
The regiment prefecture-specific fixed effect controls for all unobserved factors that are constant across the measured years, while the year fixed effects controls for all unobservable factors that are constant over the regiment prefecture cell in both the measured and the birth years. The regiment prefecture-specific time trend is included to relax the common trend assumption with respect to the cholera incidence rate. We expect the estimate $\beta$ to be statistically significantly negative.

Although internal migration across prefectures was limited at that time (Nakagawa, 2001), we cluster the standard errors at the level of nine larger areas to deal with the potential sorting effects due to internal migration (Appendix B.4 describes the detailed 9-area classification for the 47 prefectures). Therefore, our robust standard errors deal with both heteroskedasticity across areas and heteroskedasticity and correlation within areas. We also use the wild cluster bootstrap approach to estimate the variance (Cameron, Gelbach, & Miller, 2008) and confirm that our results are not disturbed by the underestimation issue because of the small number of clusters (see Appendix C.4 for the results).

### 2.3. Data

We use the height of men at age 20 as the main outcome variable in the analysis because height is an appropriate biological measure reflecting accumulated nutritional status (Fogel, 1994). The Japanese government recorded the height of most men in the military at age 20 from 1889 until the end of World War II based on the Conscription Ordinance. Our dataset is constructed from the 1899–1910 editions of the Statistical Report of the Army Ministry (SRAM), which reports the mean height of most men in the military at age 20 from 1889 until the end of World War II based on the Conscription Ordinance. Unfortunately, the 1904–1905 samples are missing because no statistics were reported during the Russo–Japanese War. Nevertheless, our comprehensive SRAM sample covers approximately 97% of the male population aged 20 at that time (see Appendix B.1 for the finer details of the data). Fig. 1 shows that although our sample experienced severe cholera pandemics in the womb from 1879 to 1890, there were few deaths from cholera during our sample period, 1899–1910. This feature lends our analysis an advantage, as the instantaneous effects via cholera exposure should not matter in our sample.

The cholera incidence rate is defined as the number of cholera patients per 1,000 people. Fortunately, we can use the incidence rate to measure exposure rather than the death rate widely used in the literature. This advantage enables us to capture the effects of pandemic cholera more precisely (Appendix C.2 also presents the results using the death rate). We confirm that the cholera incidence rate does not correlate with the lagged incidence rate (Appendix B.2). This result supports evidence of the randomness of our key variable.

Additional control variables include the coverage of hospitals, doctors, and midwives per 100 people. Medical variables are included to control for income effects and the standard of the public health environment in each prefecture. Although other socioeconomic variables in 19th-century Japan are difficult to compile, any unobserved time-constant factors such as meteorological features and agricultural productivity as well as year-specific shocks such as moderate cholera epidemics outside our exposure period (Fig. 1), macroeconomic incidence, and overall technological improvements are effectively controlled for by including the regiment-prefecture and year fixed effects. Although it is difficult to assess the mortality selection effects because of a lack of data (Bozzoli, Deaton, & Quintana-Domeque, 2009), we confirm that our main results would be unaffected by the mortality selection effects, as cholera pandemics had little reducing effects on the size of cohorts (see Appendix C.3 for the details). The summary statistics of the variables are described in Appendix B.

### 3. Results

Table 1 presents the results. Columns (1)–(7) separately include the cholera incidence rate in the two years before birth to the four years after birth. By contrast, Column (8) includes all these incidence rates at the same time to see which timing of exposure could have significant stunting effects on final height. Appendix B.2 discusses the random nature of the cholera epidemic to confirm the exogeneity of our key variables.

First, Column (1) presents the result for our falsification test using the cholera incidence rate in the two years before birth. Since the cholera pandemic in the two years before birth does not affect the fetus, this variable should not have any statistically significant effects on physical development. As expected, the estimated coefficient of this rate is near zero and insignificant. This result supports the validity of our baseline regression specification.

Columns (5)–(7) also indicate that the estimated coefficients of the cholera incidence rates more than two years after birth are statistically insignificant. By contrast, Columns (3)–(4) show that the estimated
coefficients of the cholera incidence rates in the birth year and one year after birth are negative and statistically significant at the 5% level. A similar relationship can be observed in Column (8), which presents the result for the specification that includes all the incidence variables. This result suggests that the adverse effects of cholera exposure in the birth year and one year after birth are remarkable, whereas exposure to cholera in the surrounding years is negligible in the statistical sense. Thus, our results imply that the negative impacts of pandemic cholera become clearer in early infancy than in late infancy and in utero.

We conduct several sensitivity checks including regressions using alternative specifications as well as alternative definitions of our key variable and subsample, which may not have been affected by the regulation covering the regimental district office in 1907. However, no specification produces insignificant coefficients for these two exposure variables (Appendix C.1 and C.2). Our result is also robust when using the wild cluster bootstrap procedure to deal with potential issues related to the small number of clusters (Appendix C.4).

We then calculate the magnitudes of early childhood exposure to pandemic cholera from our estimates. Column (8) argues that a one-unit increase in the cholera incidence rate in the birth year reduces the final height of men by 0.02 cm. Given that the average incidence rate in the pandemic years of 1879 and 1886 is approximately 4.3 (Fig. 1), this estimate implies that exposure to pandemic cholera in the birth year would decrease final height by approximately 0.09 cm (4.3 x 0.02). By contrast, a one-unit increase in the cholera incidence rate one year after birth reduces final height by approximately 0.03 cm. Thus, exposure to pandemic cholera in the first year of life might have decreased final height by approximately 0.12 cm (4.3 x 0.03). These magnitudes can be highlighted by calculating the magnitudes for the prefecture that experienced severe pandemics. In Toyama in 1886, the incidence rate reached 22.9, which was the maximum value throughout the Japanese archipelago at that time. The magnitudes of birth year and first year exposure are calculated to be approximately 0.46 cm and 0.66 cm, respectively. We discuss these estimated magnitudes in the next section.

4. Discussion

We found that exposure to pandemic cholera in early infancy had negative effects on adult height in industrializing Japan. Our estimates suggest that exposure to pandemic cholera led to an approximately 0.1 cm decline in the final height of men at that time. This magnitude is similar to but slightly smaller than the estimates of the influenza pandemic of 1918–1920, which led to approximately 0.1 – 0.2 cm declines in the height of both the juvenile population in prewar Japan and adult men in the United States (Mazumder et al., 2010; Ogasawara, 2017). This finding is consistent with the fact that while the pandemic cholera affected a small proportion of the population, influenza inflicted more than one in every five people.

However, one should not neglect the smaller magnitude of the effect on final height. Even such a slight decline in height could be associated with an approximately 5% higher risk of cardiovascular disease in old age (Mazumder et al., 2010). A growing body of the literature in the field of medicine has also found an association between shorter stature and the higher risk of diabetes, heart disease, and osteoarthritis (Lawlor, Ebrahim, & Davey Smith, 2002, 2004).

Our finding on the negative impacts of early childhood exposure to cholera is consistent with studies that have reported the importance of the childhood environment (Almond & Currie, 2011b). We found that the adverse effects of pandemic cholera exposure could be stronger in early infancy (ages 0 to 1) than in utero and in late infancy. This finding suggests that early infants might have been vulnerable to severe and acute dehydration due to cholera infection (Katja et al., 2006). This fact is consistent with the evidence that the negative effects of malnutrition are more obvious in early infancy than in the prenatal period and in late infancy (Neelsen & Stratmann, 2011; Ampaabeng & Tan, 2013). The unclear effects of late infancy exposure would be the acquirement of immunity for cholera in later infancy (Lyer, Bouhénia, & Rumun, 2016).

Our results provide little evidence on the adverse effects of fetal cholera exposure on the final height of men. One possible interpretation of this result is that the high fatality rate of cholera exposure (Section 2.1) wiped out the adverse effects of exposure on fetuses as healthy mothers survived. However, our regimental district-level aggregated data cannot explain the timing of exposure, which is important information when testing the fetal-origins hypothesis (Currie & Vogl, 2013). Therefore, further analyses are needed to explore the potential effects of prenatal exposure to cholera on human health. Moreover, it would also be necessary to use other indicators measuring health outcomes to offer a more comprehensive view of the effects of cholera exposure.

Despite these limitations, this study contributes to the literature by being the first to provide evidence on the negative long-run effects of pandemic cholera by using unique historical data on final height in an industrializing economy.

Supplementary data

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.ssmph.2017.11.009.

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