Effect of population density on epidemics

Ruiqi Li, Peter Richmond, Bertrand Roehner

Effect of population density on epidemics

Ruiqi Li[1], Peter Richmond[2] and Bertrand M. Roehner[3]

Abstract

Investigations of possible links between population density and the propagation and magnitude of epidemics have so far proved inconclusive. There are three possible reasons (i) A lack of focus on appropriate density intervals. (ii) For the density to be a meaningful variable the population must be distributed as uniformly as possible. If an area has towns and cities where a majority of the population is concentrated its average density is meaningless. (iii) In propagation of an epidemic the initial proportion of susceptibles (persons who have not developed an immunity) is an essential, yet usually unknown, factor. The assumption that most of the population is susceptible holds only for new strains of diseases.

Here we show that when these requirements are properly accounted for, the size of epidemics is indeed closely connected with the population density. This empirical observation comes as a welcome confirmation of the classical KMK (Kermack-McKendrick 1927) model. Indeed, one of its key predictions is that the size of the epidemic increases strongly (and in a non linear way) with the initial density of susceptibles.

An interesting consequence is that, contrary to common beliefs, in sparsely populated territories, like Alaska, Australia or the west coast of the United states the size of epidemics among native populations must have been limited by the low density even for diseases for which natives had no immunity (i.e., were susceptibles).

Key-words: epidemic, propagation, population density, Kermack and McKendrick model.

1: (a) College of Information Science and Technology, Beijing University of Chemical Technology.
Email: lir@mail.buct.edu.cn
(b) School of Systems Science, Beijing Normal University, Beijing, China.
Email: liruiqi@mail.bnu.edu.cn
ORCID: 0000-0002-3290-9476
2: School of Physics, Trinity College Dublin, Ireland. Email: peter_richmond@ymail.com
3: Institute for Theoretical and High Energy Physics (LPTHE),
University Pierre and Marie Curie/Sorbonne University,
Centre National de la Recherche Scientifique (CNRS), Paris, France. Email: roehner@lpthe.jussieu.fr

Introduction

Motivation

At the outset we note that, although the data that we analyze in this paper are mostly from the early 20th century, our objective is not to write a historical paper. We seek to explore the density effect in the propagation of epidemics in the most accurate way. Clearly, to be significant such a study must consider broad-scale epidemics of highly infectious diseases. With the possible exception of influenza, such diseases have been practically eliminated in developed countries. They still exist in developing countries but in most of these countries the reliability of vital statistics is not very good. Hence our use of early 20th century data from developed countries. In particular, data for the influenza pandemic of 1918 will provide a convenient "natural experiment".

We must also say a word about what brought us to study this question. The present investigation is a first step in an attempt to solve a long standing historical mystery which can be described as follows.

Historical accounts of the contacts between native populations and white immigrants (for instance in Pacific Ocean islands, Australia or the United States) often say, with no supporting evidence that natives were wiped out by diseases that their immune system could not fight. Such native peoples were usually living in sparsely populated areas and the question of how population density affects the propagation of epidemics becomes of central importance. The conundrum arises from the fact that if it is really true that low density hampers the propagation of epidemics (as intuition would suggest), then the disease-based explanation becomes questionable and alternative explanations must be found.

Although we briefly come back to this point in our conclusion, a more comprehensive study will be postponed to a forthcoming paper. In explaining our own motivation, our hope is to bring about further investigations by other researchers.

Milestones of the study

The investigation will proceed in four steps.

(1) Initially, convinced that it would be easy to find clear-cut results and conclusions in the literature, we were quite surprised to find mostly mixed results and it took us some time to understand the reasons for this.

(2) In a second step we found out that if the observations respect a number of appropriate requirements they lead to clear univocal results.

(3) Although reassuring, these empirical observations are for limited numbers. In order to get a picture of epidemic contagion, which has a broader validity, we

required a model based on the simplest and most natural assumptions possible and which illustrated the influence of population density. Such a model has already been proposed and studied in Kermack and McKendrick (1927). Yet, neither these authors nor their followers (e.g. Bailey 1955) paid much attention to the influence of density. Here, after a short presentation of the model, we focus on the density factor; in particular in order to make contact with the data we check that the predictions of the model are compatible. Once this confirmation has been obtained, the KMK model allows us to claim that, provided the basic assumptions on which the model relies are fulfilled, the propagation of epidemics are indeed slowed down by low population density.

(4) With this knowledge in mind we return to the question of the contacts between native populations and immigrants in the conclusion section.

What does the literature tell us?

Seen from the side of the pathogens, contagion is a form of diffusion in which the virus or bacteria jump from one individual to another. If the transmission takes place through air or water both intuition and mathematical modeling would suggest that it is facilitated by a higher population density[1]. The paradox is that in most studies that we know about, the impact of density cannot be seen clearly. This is illustrated below by the results of two studies.

Papers on influenza epidemics

In a study of the pandemic of 1918 in England and Wales (Chowell et al. 2008) the authors observe "we did not find any obvious association between death rates and measures of population density".

Similarly in a study of the same 1918 epidemic in New Zealand (Haidari et al. 2006) the authors present a plot for (x = population density, y = death rate. Although the scatter plot comprises $n = 108$ data points (each one for a separate district) the authors found that the two variables are basically uncorrelated ($r = 0.17$).

Rather than to discuss other papers (most often negative results such as the previous ones are not published) we prefer to present two observations in which one expects to see a density effect albeit none is apparent.

Influenza and pneumonia in US states

The 1918 volume of "Mortality Statistics" published by the US Bureau of the Census gives the death rate from influenza for each of the 30 Registration states i.e., the states which recorded death statistics.

[1] As a second step, at a more detailed level, one would of course expect that proximity due to specific human mobility and interactions will also play a role (Li et al. 2017a, 2017b).

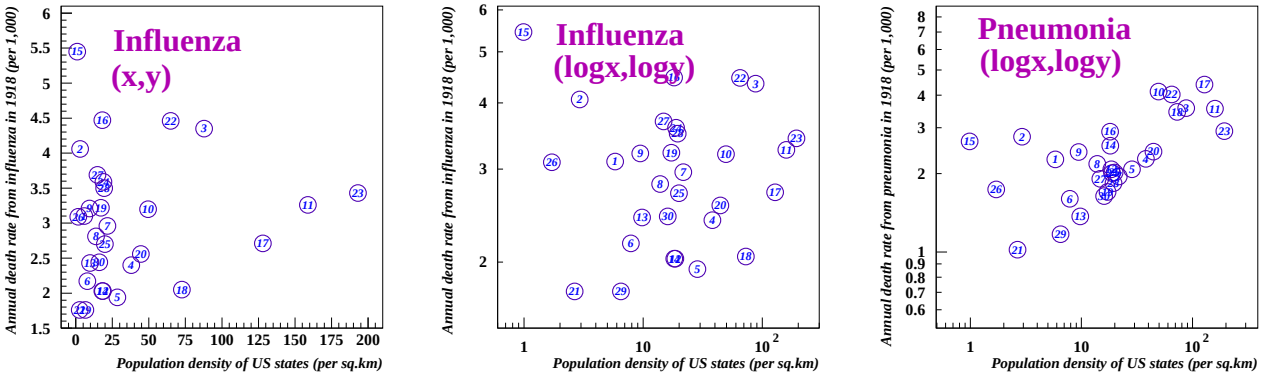

Fig. 1a,b,c Relationship between population density by state and death rate, USA, 1918. (a) This graph is for influenza. There is basically no correlation (the correlation is 0.10 and the confidence interval is $(-0.27, 0.45)$) which means that no regression line can be drawn. However, it seems (by comparison with the pneumonia case) that there are some obvious outliers such as: 15=Montana, 2=Colorado, 16=New Hampshire, 22=Pennsylvania, 3=Connecticut. It is not easy to understand why these states have death rates that are abnormally high. **(b)** The graph of (a) was redrawn with log scales The correlation, namely -0.068 is still not significant. **(c)** This graph is for pneumonia. The correlation $(\log d, \log \mu)$ is 0.62, CI$= (0.33, 0.80)$. *Sources: Density: Historical Statistics of the United States, p. 24; death rate: Mortality Statistics 1918, p.118.*

The (d =density, μ =death rate) Pearson correlation turns out to be equal to 0.10 which, for a probability level of 0.95, is not significant in the standard sense that the confidence interval, namely $(-0.27, 0.45)$ contains 0.

As a matter of fact, the scatter plot has the same shape as the one mentioned above for New Zealand: for densities under 25 per square-kilometer there is a very large dispersion of death rates; then for densities over 50 the plot becomes more orderly, yet with some outliers.

The broad range of the population density d in Fig. 1a suggests to use a log scale. For the sake of consistency (particularly in the limit $d \to 0, \mu \to 0$) it is then natural to use also a log scale on the μ axis although that is not strictly necessary on account of the narrow range of μ. This has the additional benefit that it makes the regression coefficients of $(\log d, \log \mu)$ independent of the unit of measurement used for μ.

Do these tests mean that there is no correlation whatsoever between density and death rate? Not necessarily. It simply means that the background noise overrides any weak association that may exist.

While a density effect would be expected for infectious contagious diseases, no similar effect is expected for non-contagious diseases. In other words, a comparison should show a clear-cut difference. Such a test is tried in the next subsection, once again with conflicting results.

Contagious versus non contagious diseases

Table 1 compares the death rates in large cities with those in rural areas. Here again

the results are found to be fairly puzzling. For instance, for contagious diseases, one would expect the death rate ratio cities/rural to be larger than 1. Not only is this ratio just barely higher than 1 but in addition the ratio for non-contagious diseases is markedly higher than 1. The most intriguing result is the one for pneumonia. Whereas Fig. 1c for 1918 showed a clear excess mortality in places of high density the results for 1940 (the only year for which such data are given in Linder et al. 1947) show higher death rates in rural places. In addition, if one draws the graph of death rates by states one finds that the correlation which existed in 1918 has disappeared in 1940. So, although we ignore the reason of this change, at least the two results are consistent with each other.

Table 1: Comparison of death rates in cities of more than 100,000 and in rural areas, USA, 1940

	Tubercu-losis	Pneu-monia	Syphilis	Average of contagious diseases	Intra cranial lesion	Disease of the heart	Disease of the coronary	Average of non contagious diseases
Cities	40.8	55.5	11.1		78.4	23.6	45.4	
Rural	34.0	70.0	8.80		88.0	18.6	23.0	
Cities/Rural	1.20	0.79	1.26	1.08	0.89	1.27	1.97	1.36

Notes: The death rates are per 100,000 population. There is no clear difference between cities and rural areas. The most surprising result is probably the one for pneumonia which, contrary to expectation, is notably higher in rural places (may be related to better medical treatment available in cities). As a preliminary explanation one may posit that the lower rural death rate for diseases of coronary arteries is due to the fact that life in rural places involves more physical activity.
Source: Linder et al. (1947).

Components of the background noise

To explain the observations made in Fig. 1a,b,c we used the expression “background noise”. What is the meaning intended for this expression?

An illustration from particle physics may be helpful. There are currently experiments under way to find out if protons can decay into lighter particles an idea first proposed by Andrei Sakharov (1967) in order to explain how the Big Bang has led to the present universe.

A proton decay can be identified by detecting the particles that it produces. However, in spite of the fact that in such experiments the tank is located deep under ground it is nevertheless hit by particles emitted by the Sun (especially neutrinos) or by the surrounding rocks. This is what physicists call background noise. It is different from purely statistical noise. Whereas the later cannot be reduced (except by taking averages over large numbers of events), the background noise can be reduced for instance by shielding the tank in appropriate ways. In short, the background noise is

produced by specific sources which, once clearly identified, may be eliminated.

What are here the factors which contribute to the background noise for epidemics? One can mention the following.

(1) In principle it would be better to consider incidence rates rather than death rates. By considering death rates one mixes two effects: the diffusion of the disease and the availability (and effectiveness) of medical treatment. For instance death rates from tuberculosis may be higher in poor districts where pulmonary diseases are widespread and where no treatment is provided. However, death rates may be a good proxy for incidence rates for sufficiently large areas which include wealthy as well as poor districts.

(2) The existence of large cities in an area makes the average density a fairly biased variable.

(3) The initial percentage of susceptibles which depends on the previous occurrences of the disease.

(4) The climate, whether hot or cold, dry or humid. As an illustration of how the climate effect can generate spurious data it can be mentioned that in the late 19th and early 20th centuries the dry and sunny climate of Arizona, Colorado, Nevada and New Mexico attracted many tuberculosis patients and led to the building of health facilities (sanatoriums, boarding houses and even canvas camps). Naturally, this resulted in highly inflated death rates in the corresponding states.

(5) The age structure of the population. As the 1918 epidemic hit particularly middle-aged persons, if this group is over-represented the total death rate will be higher.

The most important lesson to retain for the following sections is that one should consider *large* density changes so that their impact can overcome the background noise. As a matter of fact, Chowell et al. (2008) and Haidiri et al. (2006) also made the observation that urban areas have higher death rates than rural areas but they did not discuss the noise versus signal levels nor did they specify what must be done to make the signal stand out more clearly.

Empirical evidence for the effect of density on contagion

Overview for contagious diseases

Population density (d) is a variable with a broad range of variation, from a few persons per square kilometer in rural areas to a few thousands in big cities. In contrast, the mortality rate (μ) has a rather narrow range of variation. For this reason, if there is to be a relationship between μ and d one would expect μ to depend upon $\log d$. This is the point already emphasized in the introduction when we said that one needs

to consider large changes of d. Does this suffice to reveal a definite correlation?

Fig. 1c and Table 2 show that this is indeed true at the level of US states for several contagious diseases; yet influenza stands as an exception as shown in Fig. 1b.

Table 2: Impact of the population density d on the death rate μ of contagious diseases, US states

		Coefficient of correlation	Exponent of the power law $\mu = Cd^{\alpha}$
1	Measles, 1915	0.71	0.35 ± 0.17
	Measles, 1918	0.47	0.20 ± 0.14
	Measles, average		0.28 ± 0.11
2	Diphtheria 1915	0.67	0.24 ± 0.11
	Diphtheria 1918	0.56	0.19 ± 0.10
	Diphtheria, average		0.22 ± 0.07
3	Whooping cough, 1915	0.13	0.04 ± 0.12
	Whooping cough, 1915	0.41	0.17 ± 0.14
	Whooping cough, average		0.11 ± 0.09
4	Pneumonia, 1915	0.59	0.10 ± 0.06
	Pneumonia, 1918	0.60	0.17 ± 0.08
	Pneumonia, average		0.14 ± 0.05
5	Tuberculosis, 1915	0.39	0.12 ± 0.11
	Tuberculosis, 1918	0.48	0.15 ± 0.10
	Tuberculosis, average		0.14 ± 0.07

Notes: The correlations and regressions are for $(\log d, \log \mu)$. Taking the log of μ is not a necessity (for μ has a small range of variation) but has the advantage of making the regression independent of the way μ is measured (for example per 1,000 or 100,000). These estimates are based on the data of US registration states; there were 25 in 1915 and 30 in 1918. At this level there is no significant correlation for influenza alone; however, most often influenza and pneumonia are counted together. Apart from 1918, in all "normal" years there were about 10 times more pneumonia deaths than influenza deaths. In 1918 the two diseases had about the same death rate. Note that almost all these exponents are under 0.25 which suggest a fairly weak connection ($\alpha = 0$ would mean no connection at all).
Source: Mortality statistics 1919; this volume has a recapitulation for the years 1915 to 1919.

The results given in Table 2 show that, at least in the time period under consideration, the values of the exponent of the power law were fairly stable in the course of time. The exponent found in the next subsection for the influenza epidemic of 1918, namely 0.22 is in the same range.

It must be emphasized that exponents α in the range $0.10 - 0.25$ denote a fairly weak interdependence (obviously for $\alpha = 0$ there would be no relationship at all). That is why this effect can be easily covered by the background noise.

Influenza-pneumonia epidemic

Thanks to a special report published by the US Bureau of the Census (1920) which

describes the spread of the influenza epidemic in the fall of 1918 we have far more detailed data for this case than for any other. As in addition this epidemic was particularly strong the relative magnitude of the background noise will be reduced thus providing excellent observation conditions.

Fig. 2 summarizes the situation. Whereas there is a marked density-death rate correlation ($r = 0.90$) on a broad density scale, within rural and urban places it is the background noise which dominates.

Such scaling behavior can be used as a powerful prediction tool for the epidemic size for different population density at large scale (Li et al. 2017b).

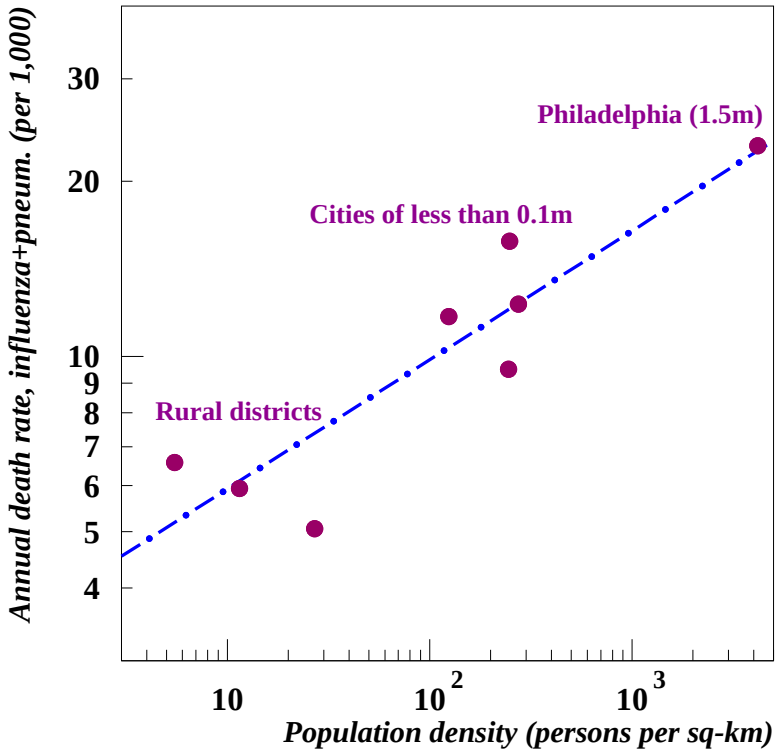

Fig. 2 Relationship between population density d and the size μ of the influenza epidemic of September-December 1918. In the graph m means million. The data are for Indiana, Kansas and the city of Philadelphia in Pennsylvania. Influenza and pneumonia deaths are counted together. It can be seen that the relationship between population density holds only on a broad density scale. Inside of the three groups of data points the background fluctuations are strong enough to override the power law. The regression reads (the confidence interval is for a confidence probability of 0.95): $\mu = Cd^{\alpha},\ \alpha = 0.22 \pm 0.08,\ C = 3.5$. *Source: Bureau of the Census (1920).*

Effect of population density on the evolution of the epidemic

There's not only a scaling relationship between population density and size of the influenza epidemic as shown above, but also a profound impact of population density on the evolution of the epidemic within cities and regions (Li et al. 2016).

Fig. 3 shows that the shape of the evolution curves is very much density dependent. Philadelphia had a much higher density than cities in Indiana and Kansas which is itself higher than the density of rural areas. As a result Philadelphia has not only a higher global mortality rate but also a higher monthly rate.

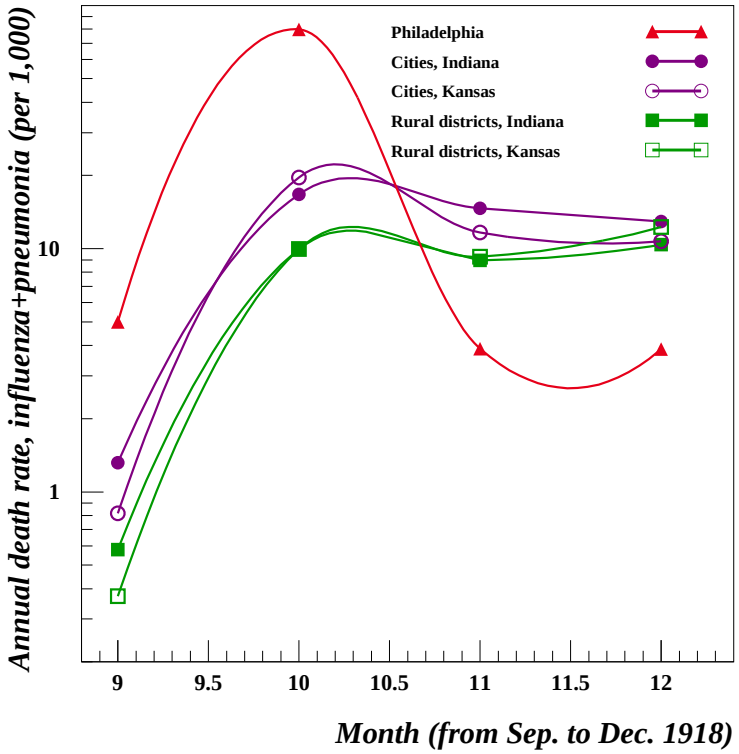

Fig. 3 Evolution of the death rate of the influenza epidemic from September to December 1918. It is remarkable that the curves for Indiana and Kansas are almost the same in spite of a distance of about 1,000 km between them; in contrast the curves are very dependent upon the population density. At the end of 1918 the epidemic was not completely over which is why the curves for Indiana and Kansas do not return to their pre-epidemic level. *Source: Bureau of the Census (1920).*

As for a big earthquake, the influenza shock of October 1918 was followed by several aftershocks, particularly in early 1919 and 1920. That is why the curves of Indiana and Kansas do not return to their pre-epidemic level in January 1919. It can also be observed that whereas the shock of October 1918 was well synchronized worldwide, the aftershocks were not the same in different continents, e.g. in Australia, Europe and North America.

Determinants of an epidemic: the KMK model

Needless to say, many epidemic models have been proposed in the course of time. Why, then do we focus our attention on the KMK model (Kermack and McKendrick

1927[2])? It is simply because it is the most basic model that can be proposed. It involves only two features: infection (through a contact between two persons) and subsequent recovery or death.

A broader presentation and discussion of the KMK model can be found in Li et al. (2016).

After defining the model our main purpose will be to see what it says about the density effect. In the original paper this aspect received a fairly short discussion only in the framework of the quadratic approximation (see below). However, as shown in Fig. 6a, this approximation is fairly poor as soon as the epidemic takes a substantial extension. As often the case with mathematicians, Kermack and McKendrick did not attempt to provide the kind of numerical solutions shown in Fig. 6a,b and Fig. 7. Thus, they may not have realized that the quadratic approximation was in fact pretty poor beyond the initial stage.

It is by purpose that the model presented in this section involves only the most basic features of an epidemic, namely contagion, recovery and death. In this way our hope is to capture and understand the key mechanism of epidemics. The fact that local conditions usually do not play a great role is demonstrated by the similarity of the course of the influenza epidemic (one of the few for which extensive daily data are available) in various cities whether in Europe or in the United States.

Mechanism and differential equations of epidemics

A simplified model of an epidemic can be seen as defined by 3 parameters (see Fig. 4)

(1) An infection (or incidence) rate, β, which describes the transition from health to illness.

(2) A removal rate, γ, which describes the transition from illness to death or recovery.

(3) A fatality rate, γ_2, which defines the proportion of deaths in the wake of the disease. The recovery rate, γ_1, will be proportional to $1 - \gamma_2$

The infection and removal effects are very different from one another

- β is determined by the type of contagion which is a biological factor but it is also highly dependent upon the frequency of inter-individual contacts[3]. It can be expected to be small when the population density is low.

[2]Their study was in three parts: Kermack and McKendrick (1927, 1932, 1933). Although in the reference section we cite all three papers we are in fact only interested in the first one because the two others include a number of less basic features. It can be noted that the three papers were reprinted in 1991 in the "Bulletin of Mathematical Biology". This model is still in use nowadays; sometimes it is referred to as the SIR model where SIR means Susceptible-Infected-Recovered. Li et al. (2016) gives a full introduction to this class of models.

[3]The relationship between the network structure of the population and the frequency of interactions was examined in Li et al. (2013).

- γ describes the evolution of the disease either to death or to recovery. Thus, it is chiefly a biological parameter which is dependent upon the type of the disease.

In the argument which leads to the equations defining the model the crux of the matter is the fact that newly infected persons are generated through interaction between a person that is already infected (described by the variable y) and a susceptible person, i.e., a person not yet infected and who has not yet developed an immunity (described by the variable x). In the differential equation of the model this interaction is described by a product term βxy where β describes the infection process. As the disease progresses the pool of infected persons is depleted because infected persons may die or may recover and then be immune at least for the near future. This removal process will be described by a term $-\gamma y$. In other words there is a competition between infection and removal which can be quantified by the ratio $\rho = x_0\beta/\gamma$.

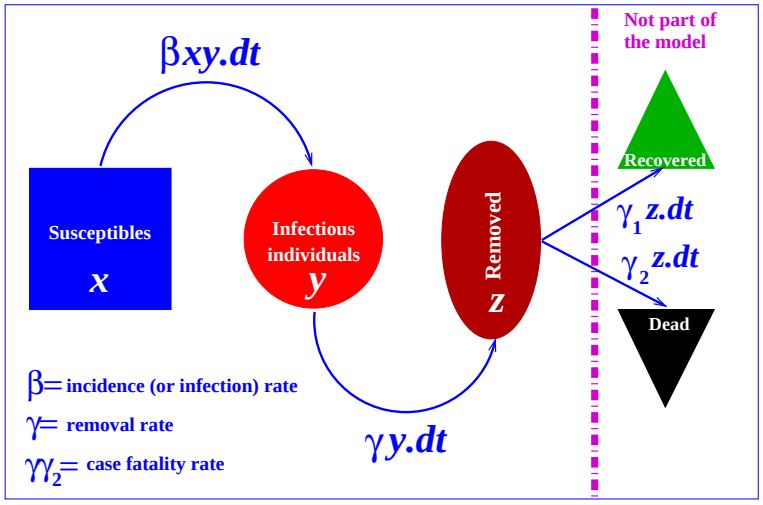

Fig. 4 Diagram illustrating the mechanism of the KMK model (Kermack and McKendrick 1927) for the propagation of an epidemic. $x(t)$ =persons susceptible to infection, $y(t)$ =infected (and infectious) persons, $z(t)$ =persons who have been infected and who, at time t are either dead or immune to infection.

This is summarized in the following system of differential equations.

$$(1)\quad \begin{cases} dx/dt &= -\beta xy & & & x: \text{ susceptibles (i.e. never infected)} & (1.1)\\ dy/dt &= \beta xy & - & \gamma y & y: \text{currently infectious} & (1.2)\\ dz/dt &= & & \gamma y & z: \text{ once infected, now dead or immune} & (1.3) \end{cases}$$

In addition it should be added that $x + y + z = n$ and that we are only interested in non-negative solutions, that is to say: $x(t), y(t), z(t) \geq 0$.

Main features of the epidemic: how does it work

One can make three simple, yet quite useful, preliminary observations.

(1) As x, y, z are non-negative, equation (1.1) and (1.3) show that x can only decrease whereas z can only increase. Thus, after the process has started from an initial situation where $x_0 \simeq n,\ y_0 \simeq 0,\ z_0 = 0$ the variable $x(t)$ will fall and $z(t)$ will grow. Until when will this go on? The answer is given by equation (1.2).

(2) At time $t = 0$ equation (1.2) becomes: $dy/dt = (\beta x_0 - \gamma)y_0$. Clearly the right-hand side must be positive for otherwise the process cannot start; this implies: $x_0\beta/\gamma > 1$. This quantity plays an important role, we call it the *threshold parameter* $\rho = x_0\beta/\gamma$.
Then, when x decreases, at one point $x(t)$ will become equal to γ/β; after that it cannot fall further. In other words, the process will stop. Thus, the propagation of the epidemic stops well before $x(t)$ becomes zero that is to say before the whole population has been infected. In other words, under the assumptions made here a population cannot be completely wiped out by an epidemic (even if $\gamma_1 = 0$). We will come to the same conclusion below when we discuss the variable z.

(3) Whereas the meaning of the variables x and z appears fairly clearly, from a practical perspective the meaning of y is less clear. However, equation (1.3) tells us that y is proportional to dz/dt and the later has a clear practical interpretation. If, for the sake of simplicity we assume that all infected people die (which means that in Fig. 4 γ_1 is zero), then dz/dt represents the daily (or weekly) number of deaths. This is a quantity commonly recorded in any epidemic.

Reduction to a single differential equation

The system (1) can in fact be reduced to a single nonlinear equation. From (1.1) and (1.3) follows: $dx/dz = -\beta x/\gamma$ which implies: $x = x_0 \exp(\beta z/\gamma$. Replacing this in (1.3) one gets:

$$\frac{dz}{dt} = \gamma\left[n - z - x_0 \exp\left(-\frac{\beta}{\gamma}z\right)\right] \tag{2}$$

By expanding the exponential to second order one gets a logistic equation which can be solved analytically. This quadratic approximation is valid when $\beta/\gamma \ll 1$ and remains valid as long as z is small enough.

Outcome of the epidemic for $t \to \infty$

When $t \to \infty$ the variable $z(t)$ which represents the persons affected by the epidemic converges toward a stationary limit which is the solution of the equation:

$$n - z = x_0 \exp\left[-\rho(z/x_0)\right] \tag{3}$$

Fig. 5 shows that the limit of z increases when ρ becomes larger. The way the size of the epidemic increases with ρ is shown more precisely in Fig. 6b which is based on a numerical solution of equation (2).

Can a population be wiped out by an epidemic?

The death toll of the epidemic is described by the parameters γ_1, γ_2 of Fig. 4. Although this part of the process is not covered by the model, it is nonetheless possible to determine if a population can be wiped out for even in the worst case (i.e. $gamma_1 = 0$) the death toll cannot exceed $z(\infty)$.

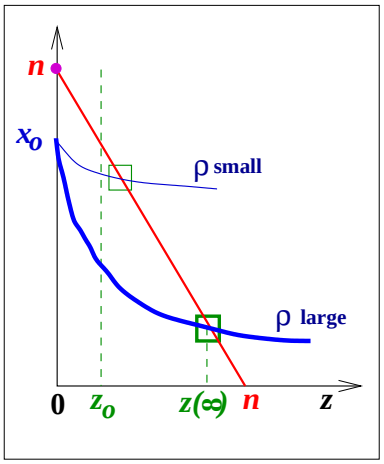

Fig. 5 Limiting value of the variable z which represents the total number of persons who have been infected. The straight line represents the left-hand side of equation (3) whereas the curve represents the exponential in the right-hand side of the same equation. The intersections marked by the green squares correspond to the asymptotic value $z(t \to \infty)$. The figure shows two things: (i) $z(\infty)$ is always smaller than n which means that there are always some persons which are not infected. (ii) $z(\infty)$ increases along with the threshold parameter $\rho = x_0\beta/\gamma$. It can also be noted that because of the relation $x + y + z = n$ the interval $n - x_0$ is equal to $y_0 + z_0$; this allows a discussion of the solutions according to various cases of initial conditions.

Both Fig. 5 and Fig. 6b show that, whatever the values of the parameters β, γ, $z(\infty)$ is always smaller than the whole population n. In other words, under the present assumptions, a population *cannot* be wiped out by an epidemic. Even if all infected persons die (which would correspond to a very severe disease and a complete lack of immunity) non-infected persons will remain alive. This is because as the number of dead people increases at the same time the sources of infection (i.e. the y) dwindle.

In short, no matter the severity of a disease only a fraction of the population will die, although it is true that this fraction may become close to one when ρ becomes large.

The situation would be different if the dead are not buried and remain a source of contagion. Although this case is not covered by the present model, one can imagine that in such a case the whole population can be wiped out.

Key-role of population density

The threshold parameter $\rho = x_0\beta/\gamma$ is proportional to the initial number of susceptibles which itself, in case of a new disease, is close to the total population. The model does not describe the spatial aspects of the epidemic but as it is formulated for a population n on a given territory it implies that population density and total population are both proportional to n. In other words, n plays the role of population density.

Fig. 6b shows how the size of the epidemic increases with the threshold parameter that is to say, provided $x_0 \simeq n$, with population density.
In the real world, one expects β also to increase with population density. As ex-

plained earlier, β depends upon the number of contacts and one expects people to have more interactions (in stores, public transportation, entertainment places or at work) in cities than in rural places. Needless to say, the level of β in cities depends upon the special features of the city[4]. For instance, because of the difference in public transportation one would expect β to be higher in Tokyo than in Los Angeles.

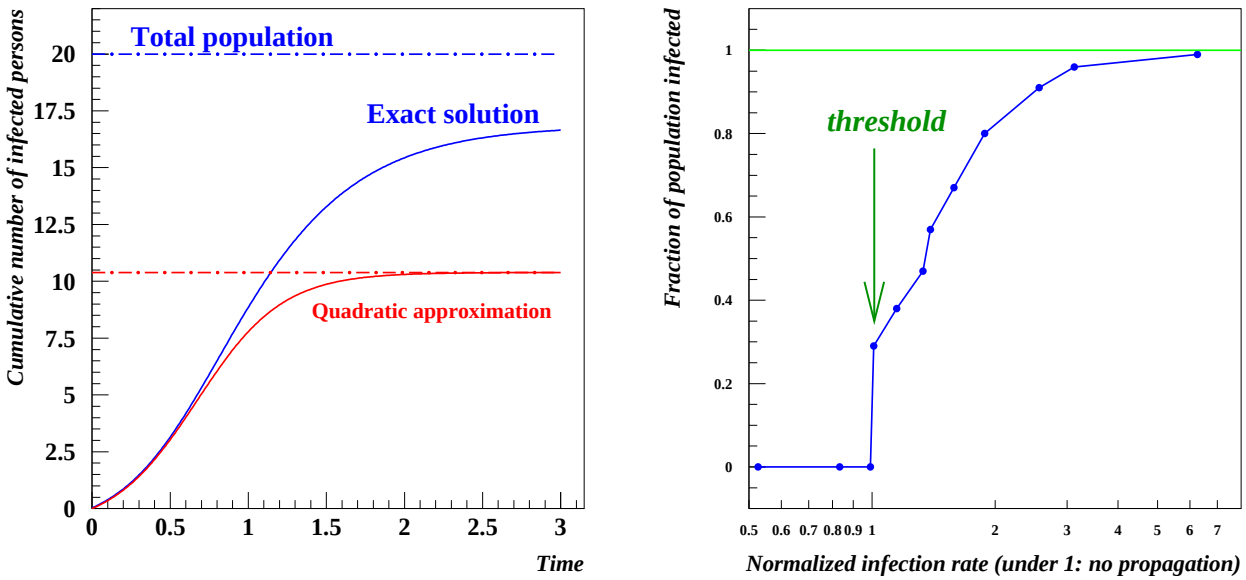

Fig. 6a,b The KMK model. (a) Increase in time of the fraction of the population which has been in contact with the disease. This simulation corresponds to the following parameters: total population: $n = 20$, $x_0 = n - 1$, $\beta = 0.32$, $\gamma = 3$, $\rho = x_0\beta/\gamma = 2.03$. The model's equations must be solved numerically, but there is also an analytic approximation which is shown by the lower curve. The accuracy of this approximation is controlled by the threshold parameter ρ. When ρ is slightly larger than 1, the infection starts slowly and only a small fraction of the population becomes infected. **(b)** This graph shows the total fraction of the population that has become infected, that is to say $z(\infty)/n$, as a function of $n\beta/\gamma$ that we call the "normalized infection rate". When $n \simeq x_o$ it becomes identical to the threshold parameter ρ. We have seen that the epidemic can develop only if this parameter is larger than 1.

Remark

It can be added that the increase of the size of the epidemic with the density is specific to the exact model. In the quadratic approximation (which results in a logistic equation for $z(t)$) the size of the epidemic (that is to say the limit of $z(t)$ when t goes to infinity) is given by the expression:

$$z(\infty) = 2\gamma/(x_0\beta)\,[x_0 - \gamma/\beta]$$

which, obviously, does not increase with x_0.

Comparison to observation

[4]The hydrological environment plays a major role in the spreading of cholera. More generally, the role of population distribution and of human interaction intensity was examined in Li et al. (2017 a,b).

The “Special Report” (Bureau of the Census 1920) gives death rates by month. In a few instances it gives also daily death data which provide a more accurate view of the shape of the curve which describes the time evolution of the epidemic.

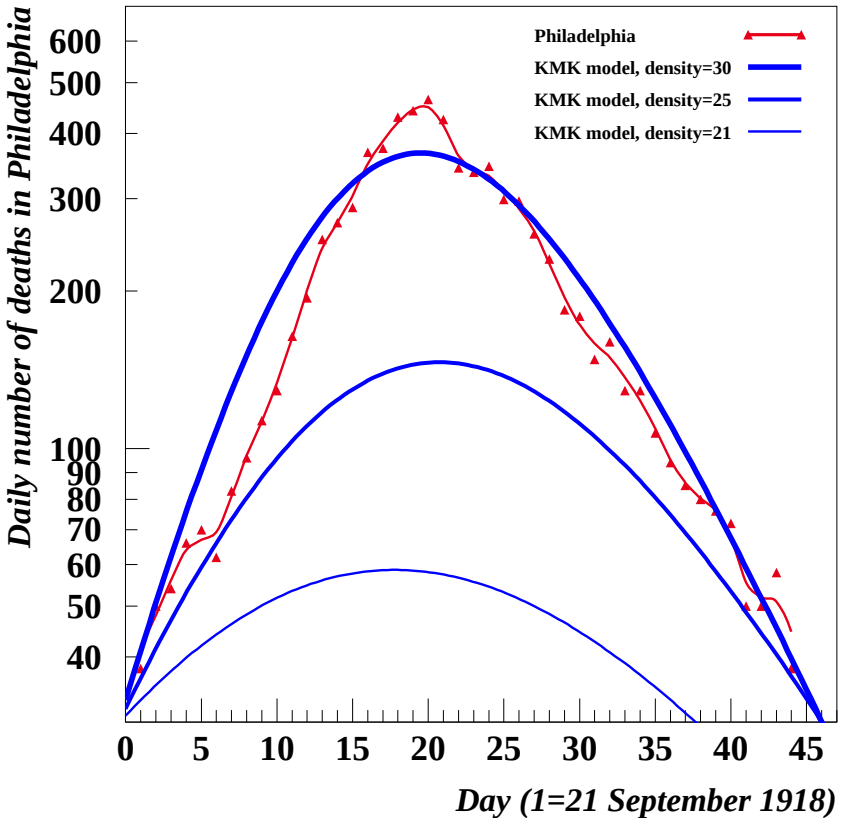

Fig. 7 Predictions of the KMK equations for different densities and comparison with daily deaths in Philadelphia. It can be seen that for the model as well as for Philadelphia the raising and falling parts are nearly exponential. Apart from the population n, the other parameters have the following values: $\beta = 0.32$, $\gamma = 5$, $x_0 = n - 1$, $y_0 = 1$, $z_0 = 0$. At its peak the amplitude of the daily number of deaths increases as $d^{5.2}$. *Source: The daily data for Philadelphia are from: Bureau of the Census (1920).*

In Fig. 7 we tried to determine parameters which would lead to this shape. The height of the peak can be easily controlled through the threshold parameter; this is shown in fig. 7 by the three curves corresponding to different densities. However, a larger ρ will give a curve whose falling part is wider than its raising part whereas in fact the empirical curve is almost symmetrical with respect to its peak value. The descending part can be made shorter by increasing γ. In this way, we can define a set of parameters which approximates fairly closely the empirical curve.

Predictions of the model

From a mathematical perspective, one of the model’s distinctive features is the existence (shown in Fig. 6b) of a threshold under which the death rate falls abruptly to zero. In other words for sufficiently low densities one should see a sudden drop

of the death rate. Practically, however, what we can see in the low density range is limited by the noise. In our comments about Fig. 2 we have already observed that for rural places the impact of the density is over-ridden by the noise. Note that the problem of the noise is more serious for low densities than for high densities because low densities means few deaths which in turn imply high statistical fluctuations. As observed in the first section, such fluctuations come in addition to the background noise.
In other words, it will be difficult to ever observe the nice phase transition that is supposed to occur at the threshold density.

However, this does not really matter. From our perspective, what is important is the fact that the severity of the epidemic increases rapidly with the density. Fig.7 and similar simulations for other values of β and γ show that, as a function of density, the maximum M of the time series increases as a power law: $M \sim d^{\nu}$. Not surprisingly, the exponent ν of this law is itself a function of β and γ. For instance, when $\gamma = 5$, ν increases rapidly from 0 to 3 when β increases from 0 to 0.30 and then it decreases slowly for values of β larger than 0.30.

Conclusion

Main results and open questions

We have shown that there is a weak but clearly defined relationship between population density and the death rate of epidemics providing sufficiently large density ranges are considered and background noise is kept under control. We have also shown that population density determines the time dependence of the death rate; thus, large densities (as in Philadelphia) lead to high narrow peaks whereas for small densities one observes low and broad humps.

The question of the length of time of an epidemic process deserves a closer study. Here we have considered only influenza and pneumonia, diseases for which the incubation time and the length of survival may be as short as a few days. However, for other diseases these times may be much longer: for rabies it is a few months, for AIDS a few years[5].

In a recent paper (Richmond et al. 2018) a methodology was developed which allows measurement of the strength of family interactions between spouses or between parents and children. One may wonder whether the propagation of a disease can serve to estimate the proximity between family members and more broadly between people. At the moment one can only say that this requires detailed epidemic microdata that

[5]Rabies and AIDS have specific spreading mechanisms which should be taken into account in any model description.

seem not to be available.

Immigration shock in native populations

Finally, let us briefly discuss the question of the immigration shock in the light of what we have learned in the present study.

Epidemics ascribed to a lack of immunity in native populations are often given as the reason of their collapse. The following excerpt taken from Marsh (2004) is typical of this kind of statements:

> "Nevada Indians had no immunity to the diseases that white explorers, colonists and settlers brought to their lands. These diseases included smallpox, measles, tuberculosis and others, which ravaged the tribes in great epidemics that killed many, and sometimes all, members of a tribe".

From a scientific point of view such statements are unsatisfactory for several reasons.

(1) Together with the death of some in the community comes immunity for those who survive.

(2) Quite as important as the death rates are the birth rates. Often in the wake of an epidemic or famine there is a birth rate rebound. This is well documented after the famines in India in the 19th and first half of the 20th century (Maharatna 1992).

(3) It is not easy to determine the moment when a native population has come in contact with persons who may carry pathogens. For instance, it is abundantly clear that the Nevada Indians had contacts with Spanish people for a long time before the area became part of the US following the Mexican-American War of 1846-1848. The main difficulty is that the paucity of sources does not allow us to set contact dates in a reliable way[6].

(4) Most often native populations have low density. This is of course true for the Nevada Indians. If one takes $d = 1$ person per sq.km as a rough density estimate of native populations[7] and $d = 340$ as the density of present-day Massachusetts, then according to Table 2 the death rate due to a contagious disease will be $340^{0.20} = 3.2$ times smaller in the native population. From Table 2 we know that the exponent is slightly disease-dependent; the value of 0.20 taken here represents a rough average. Thus, one would expect diseases to be less severe in low density areas like Alaska, Arizona or Nevada.

(5) Usually for native populations there are neither census records nor reliable estimates. However, in a few cases there are acceptable data going back to the early

[6] Actually, the very definition of the notion of "contact" is unclear. Is the arrival of one or several hunters sufficient to start an epidemic? We do not know.

[7] It is almost impossible to know the population density of Arizona, California, Nevada or New Mexico around 1850 because at that time American Indians were not counted in US censuses. The 1890 census was the first to include the enumeration of all Indians. See: https://www.census.gov/library/publications/1864/dec/1860a.html.

19th century; Alaska and the Tonga Islands in the Pacific are two such cases and, remarkably, their population did not experience any collapse after coming into contact with white travelers. Below we give some additional details for Alaska.

(6) There are indeed documented cases of sudden population collapses within two or three decades. If diseases are not the right explanation how can one explain them? There are plenty of possible reasons: starvation or malnutrition when the traditional source of food (e.g., salmons, buffaloes) is no longer available, dispersion of tribes and splitting of families which prevents conceptions, or outright killings. Such events can occur simultaneously as documented by Benjamin Madley (2008, 2016) for the California Indians.

For the case of the Alaskan Indians there are two conflicting accounts: Mooney (1929) claims a sharp population fall due to diseases over the period 1740-1780, a time interval for which there are in fact no data available whereas for Petroff (1884) who based his account on the Russian population estimates which became available after 1780 there was no sizable population decrease. Note that the tribes of continental Alaska came into contact with white people only by 1840. In other words, in this case one does not observe any substantial immunity shock.

References

Bailey (N.T.J.) 1955: Some problems in the statistical analysis of epidemic data. Journal of the Royal Statistical Society B 17,35-68.

Bureau of the Census, Special Report 1920: Special tables of mortality from influenza and pneumonia. Indiana, Kansas, and Philadelphia, September 1 to December 31, 1918. Government Printing Office, Washington DC.

Chowell (G.), Bettencourt (L.M.A.), Johnson (N.), Alonso (W.J.), Viboud (C.) 2008: The 1918-1919 influenza pandemic in England and Wales: spatial patterns in transmissibility and mortality impact. Proceedings of the Royal Society B, 7 March 2008.

Haidari (A.A.), Hazmi (A.A.), Marzouq (H.A.), Armstrong (M.), Colman (A.), Fancourt (N.), McSweeny (K.), Naidoo (M.), Nelson (P.), Parnell (M.), Rangihuna-Winekerei (D.), Selvarajah (Y.), Stantiall (S.), Wilson (N.), Baker (M.) 2006: Death by numbers. New Zealand mortality rates in the 1918 influenza pandemic. Publication of the Wellington School of Medicine and Health Sciences.

Kermack (W.O.), McKendrick (A.G.) 1927: Contributions to the mathematical theory of epidemics, I. Proceedings of the Royal Society, A, 115,700-721.

Kermack (W.O.), McKendrick (A.G.) 1932: Contributions to the mathematical theory of epidemics, II. The problem of endemicity. Proceedings of the Royal Society, A, 138,55-83.

Kermack (W.O.), McKendrick (A.G.) 1933: Contributions to the mathematical theory of epidemics, III. Further studies of the problem of endemicity. Proceedings of the Royal Society, A, 141,94-122.

Li (R.), Tang (M.), Hui (P.-K.) 2013: Epidemic spreading on multi-relational networks. Acta Physica Sinica, 62,16,168903.

Li (R.), Wang (W.), Shu (P.), Yang (H.), Pan (L.), Cui (A.), Tang (M.) 2016: Review of Thresold analysis about epidemic spreading dynamics on complex networks. Complex Systems and Complex Science 13,1-39.

Li (R.), Wang (W.), Di (Z.) 2017a: Effects of human dynamics on epidemic spreading in Côte d'Ivoire. Physica A, 467,30-40.

Li (R.), Dong (L.), Zhang (J.), Wang (X.), Wang (W.-X), Di (Z.), Stanley (H.E.) 2017b: Simple spatial scaling rules behind complex cities. Nature Communications, 8,1841.

Linder (F.E.), Grove (R.D.) 1947: Vital statistics rates in the United States, 1900-1940. National Office of Vital Statistics, Government Printing Office, Washington DC.

Madley (B.) 2008: California's Yuki Indians. Defining genocide in native American history Western Historical Quarterly 39,3,303332.

Madley (B.) 2016: An American Genocide. The United States and the California Indian Catastrophe, 1846-1873. Yale University Press, New Haven.

Maharatna (A.) 1992: The demography of Indian famines: a historical perspective. Thesis, London School of Economics and Political Science. University of London.

[In 1996 the thesis was published by Oxford University Press (Dehli) under the title: "The demography of famines: an Indian historical perspective."]

Marsh (C.) 2004: Nevada native Americans. Galopade International.

Mooney (J.) 1929: The aboriginal population of America north of Mexico. Smithsonian Miscellaneous Collections Vol.80, No 7,1-40.

Petroff (I.) 1884: Report on the population, industries, and resources of Alaska. Prepared at the request of the US Bureau of the Census.

Richmond (P.), Roehner (B.M.) 2018: Exploration of the strength of family links. Physica A 502,1-13.

Sakharov (A.) 1967: Violation of CP invariance, C asymetry and baryon asymetry JEPT Letters (Journal of Experimental and Theoretical Physics Letters) 5,24-26.