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LIMIT THEORES FOR THE GENERALIZED SIZE OF THE EPIDEMIC IN ONE MARKOV'S EPIDEMIC MODEL WITH IMMUNIZATION AND TAKING INTO ACCOUNT THE INHOMOGENEITY OF MIXING

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Abstract. A new Markov model of epidemic spread in a closed population is introduced, where, in addition to standard transitions reflecting infection process of individuals and eliminating of infection sources, we also introduce a transition associated with immunization of individuals. While in the known model with natural immunization the probability of a last transition is proportional to the number of possible contacts between infected and uninfected individuals, in the model we consider this probability is proportional to the number of infected individuals only, that is, as the number of infected individuals increases, the probability of immunization also increases.

For different values of the initial parameters of the introduced model, the class of limit laws for the generalized extension of the epidemic (the number of infected individuals plus the number of immunized individuals at the end of the epidemic) is described under the assumption that the initial number of infected and uninfected individuals tends to infinity and the parameters depend on them ("Series scheme"). (at most 150 words)

1. Introduction

We introduce the following Markov model of the development of an epidemic in a closed population, with the help of which we can compare the previously known models with the model considered in this article. Let $\xi(t) = (R(t), S(t))$ -the state of the population at a given time $t \geq 0$,where R(t) -number of susceptible,and S(t) -number of sources of infection at a time t,moreover $\xi(0) = (n, m)$. We define the Markov model of the spread of the epidemic using the following probabilities of possible transitions beyond infinitesimal period of time Δt

$$\begin{cases} P(\xi(t+\Delta t) = (r-1, s+1)/\xi(t) = (r,s)) = \lambda\varphi_1(r)\psi(s)\Delta t + o(\Delta t), \\ P(\xi(t+\Delta t) = (r, s-1)/\xi(t) = (r,s)) = \mu\psi(s)\Delta t + o(\Delta t), \\ P(\xi(t+\Delta t) = (r-1, s)/\xi(t) = (r,s)) = \theta\varphi_2(r)\psi(s)\Delta t + o(\Delta t), \end{cases} \tag{1.1}$$

where the first and second transitions reflect the process of infection of susceptible and elimination of patients, respectively, and the third transition is the process of immunizing susceptible ones.

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The classical, so-called general probabilistic model, was proposed in 1927 and is associated with the names English scientists Kermack and McKendrick [1].This model is obtained from (1.1) for $\varphi_1(r) = r$, $\psi(s) = s$, $\varphi_2(r) = 0$.It was further thoroughly investigated by Bartlett [2], and the process itself was called the Bartlett-McKendrick process (see, for example, [3]).

A more generalized model with $\varphi_1(r) = r$, $\psi(s) = s$, $\varphi_2(r) = r$ was reviewed by Downton in 1968 [4] and independently of him Nagaev A.The. and Rachmanina G.I. in 1970 [5], in the last of which the third transition has been interpreted as natural immunization, i.e. it reflects the possibility of the transition of the susceptible to the number of immunized as a result contact with the source of infection.

For Bartlett's general probabilistic model [2] established the Kolmogorov equation for the generating function of the probabilities of the process states

$$\Pi_t(z,w) = \sum_{r=0}^{n} \sum_{s=0}^{\alpha+n-r} P(\xi(t) = (r,s)) z^r w^s, \tag{1.2}$$

which looks like this:

$$\frac{\partial \Pi_t(z,w)}{\partial t} = (w^2 - zw)\frac{\partial^2 \Pi_t(z,w)}{\partial z \partial w} + \rho_1(1-w)\frac{\partial \Pi_t(z,w)}{\partial w}, \tag{1.3}$$

where $\rho_1 = \mu/\lambda$ -is the relative coefficient of elimination. In 1965, equation (1.3) was solved explicitly independently of each other by Ghani [6] and Siskind [7]. An equation of type (1.3) with explicit coefficients at the derivatives turned out to be solvable only due to the special form of the unknown function $\Pi_t(z,w)$.

Unfortunately, the explicit form of the solution of equation (1.3) is so cumbersome that it is difficult to subject it to any asymptotic analysis, as well as to reveal the ratios of the initial parameters characteristic of a particular behavior of the process.In this regard, attempts were made (both before obtaining an explicit solution to the model and after that) asymptotic analysis of the model mainly regarding the distribution of epidemic size in a large population ($n \to \infty$). The most general approach to the asymptotic analysis of the distribution of this most important functional was taken in the works of A.V. Nagaev. and his students since 1968 ([9], [10],[11] and etc).In these works, a method was developed for reducing the problem of the distribution of the size of the epidemic to a boundary problem for the sums of independent random variables in the series scheme.

In this paper, we carry out a similar asymptotic analysis of model (1.1) for $\varphi_1(r) = r^a$, $\psi(s) = s$, $\varphi_2(r) = 1$, where a is the probability of infection of a susceptible person upon contact with a source of infection. In contrast to the general probabilistic model and the model with natural immunization, specific difficulties arise in the implementation of boundary problems, as well as new effects in the ratio of the initial parameters.As for the explicit solution of the equation for the generating function in the model under consideration, as well as in the model with natural immunization, this question still remains open, but, nevertheless, the question of asymptotic analysis, by virtue of the above, remains relevant. [12]-[14].

We also note that the asymptotic analysis of the non-Markov analogue of the general probabilistic model, which takes into account the state of the immune system of the susceptible, and the infectious period is arbitrary (other than indicative) distribution, was further considered in works [12]-[14].

2. Problem statement and formulation of results

Thus, the work will consider the following Markov model of the development of the epidemic

$$\begin{cases} P(\xi(t+\Delta t)=(r-1,s+1)/\xi(t)=(r,s))=r^{\alpha}s\Delta t+o(\Delta t),\\ P(\xi(t+\Delta t)=(r,s-1)/\xi(t)=(r,s))=\rho_1 s\Delta t+o(\Delta t),\\ P(\xi(t+\Delta t)=(r-1,s)/\xi(t)=(r,s))=\rho_2 s\Delta t+o(\Delta t), \end{cases} \tag{2.1}$$

where $\rho_1=\mu/\lambda$, and $\rho_2=\theta/\lambda$ - the relative rates of elimination and immunization, respectively.

Values will act as regulating parameters $\theta_1=\rho_1/n$ and $\theta_2=\rho_2/n$, in relation to which the classification of various cases of process behavior will be carried out.

It is clear from the definition that states of the form $(k,0)$, $0\le k\le n$ are absorbing for the process $\xi(t)$.

The object of the study will be the generalized size of the epidemic $\nu=\nu_1+\nu_2$,where ν_1 and ν_2 -the number of those who had recovered and were immunized susceptible to the end of the epidemic.

Throughout what follows in this work, it will be assumed that $m\to\infty$, $n\to\infty$, $m=o(n)$,and also that $\lim\limits_{n\to\infty}\theta_2=\theta_{20}$, $0\le\theta_{20}<\infty$. Moreover, with respect to the parameter θ_1 the transition case of the 1st type will be considered:$\lim_{n\to\infty}\theta_1=\theta_{10}=1$.

For this case, the following preliminary general comments can be made.In a transitional case of type 1, at the initial stage of the development of the process, the number of initial patients will change (provided that the change has occurred) by +1 or -1 with probabilities close to 1/2, i.e. the process has no tendency (trend) and absorption occurs due to random fluctuations, and the absorption probability itself is approximated by the probability of the first exit by the Wiener process of a certain smooth boundary.This happens with a relatively fast aspiration θ_1 to 1 so that $1-\theta_1=O(1/m)$.

Let's start formulating the results.The symbol $\Longrightarrow$ everywhere means weak convergence.

Theorem 2.1. *If* $\theta_1\to 1$, $\beta\equiv m(1-\theta_1)\to\beta_0$, $\frac{m^3}{n}\to\gamma_0<\infty$, $\mid\beta_0\mid<\infty$, *then for any fixed* $x¿0$

$$P\left(\nu>\frac{(1+\theta_2)m^2}{2}x\right)\Longrightarrow$$

$$\Longrightarrow P\left(w(t)<\frac{1}{\sqrt{x}}+\beta_0\sqrt{\frac{x}{2}}t-\frac{(1+\theta_{20})\gamma_0 x^{\frac{3}{2}}}{4\sqrt{2}}t^2\ ,\ 0\le t\le 1\right).$$

where $\omega(t)$ *-standard Wiener process.*

Consequence 1. If $\gamma_0 = 0$, then under the conditions of Theorem 1,

$$P\left(\nu > \frac{(1+\theta_2)m^2}{2}x\right) \Longrightarrow 1 - e^{\frac{-(\beta_0+|\beta_0|)}{\sqrt{2(1+\theta_{20})}}} \int_0^{\beta_0^2/4(1+\theta_{20})} p(u)du,$$

where $p(u) = \dfrac{\mid \beta_0 \mid e^{\frac{|\beta_0|}{\sqrt{2(1+\theta_{20})}}}}{2\sqrt{2\pi(1+\theta_{20})}} u^{-3/2} e^{-u-\beta_0^2/8u(1+\theta_{20})}$.

Consequence 2. If in addition $\beta_0 = 0$, then

$$P\left((1+\theta_2)m^2x/2\right) \Longrightarrow \sqrt{\frac{2}{\pi}} \int_0^{1/\sqrt{x}} e^{-u^2/2}du.$$

3. Reduction to a boundary value problem for sums of independent random variables

The general scheme of the proof is close to the works [5] and [10].Absorption of the Markov process (2.1) into the state (n-k, 0) corresponds to the generalized size of the epidemic $\nu = k$ and so to study this distribution, it is sufficient to restrict ourselves to considering the corresponding embedded Markov chain:

$$\begin{cases} P\left((r,s) \to (r-1, s+1)\right) = \left(\frac{r}{n}\right)^a / (\theta_1 + \theta_2 + \left(\frac{r}{n}\right)^a) \ , \\ P\left((r,s) \to (r, s-1)\right) = \theta_1 / \left(\theta_1 + \theta_2 + \left(\frac{r}{n}\right)^a\right) \ , \\ P\left((r,s) \to (r-1, s)\right) = \theta_2 / \left(\theta_1 + \theta_2 + \left(\frac{r}{n}\right)^a\right) \ . \end{cases}$$

It should be noted that a similar random walk in the case of a general probabilistic model was introduced by Foster [15].

For convenience, we pass to an equivalent random walk using the transformation $r' = n - r$, $s' = n - r - (s - m)$:

$$\begin{cases} P\left((r',s') \to (r'+1, s')\right) = \dfrac{\left(1-\frac{r}{n}\right)^a}{\theta_1 + \theta_2 + \left(1-\frac{r}{n}\right)^a} = p^{(1)}_{nr'} \ , \\ P\left((r',s') \to (r', s'+1)\right) = \dfrac{\theta_1}{\theta_1 + \theta_2 + \left(1-\frac{r}{n}\right)^a} = p^{(2)}_{nr'} \ , \\ P\left((r',s') \to (r'+1, s'+1)\right) = \dfrac{\theta_2}{\theta_1 + \theta_2 + \left(1-\frac{r}{n}\right)^a} = p^{(3)}_{nr'} \ . \end{cases} \tag{3.1}$$

It is easy to see that the walk (3.1) starts at the point (0,0), and the integer points of a straight line $s' = m + r', r' = 0, \ldots, n$.

Next, we introduce auxiliary random variables ξ_{ni} as the residence times of a wandering particle at straight $r' = i - 1, i = 1, 2, \ldots, n$.It is easy to understand, since the walk (3.1) is Markov, that these r.v. independent and geometrically distributed

$$P(\xi_{ni} = k) = (1 - p^{(2)}_{ni-1})(p^{(2)}_{ni-1})^k, k = 0, 1, \ldots, n. \tag{3.2}$$

In addition, we introduce the random variables η_{ni},which take the value 1 if the transition to the line $r' = i$ occurred by immunization susceptible and 0 if it was carried out by disease, i.e.

$$\eta_{ni} = \begin{cases} 1 \ , \ \frac{\theta_2}{\theta_2 + \left(1 - \frac{i-1}{n}\right)^a} \ , \\ 0 \ , \ \frac{\left(1 - \frac{i-1}{n}\right)^a}{\theta_2 + \left(1 - \frac{i-1}{n}\right)^a} \ . \end{cases} \tag{3.3}$$

It is easy to understand that random variables $\eta_{n1}, \eta_{n2}, \ldots . \eta_{nn-1}$ will also be independent.Note also that in the model with natural immunization, the random variable η_{ni} takes values 1 and 0 with probabilities $\theta/(\lambda+\theta)$ and $\lambda/(\lambda+\theta)$ respectively.

Now we introduce the basic random variables

$$\xi_{n1} = \zeta_{n1} \ , \ \xi_{ni} = \zeta_{ni} + \eta_{ni-1} \text{ if } i \geq 2.$$

It is easy to establish from (3.2) and (3.3) that

$$P(\xi_{ni} = k) = \begin{cases} p^{(1)}_{ni-1} \ ,\text{if } k = 0, \\ (1 - p^{(1)}_{ni-1})(1 - p^{(2)}_{ni-1})(p^{(2)}_{ni-1})^k \ , \text{ if } k \geq 1. \end{cases} \tag{3.4}$$

Next, we introduce the sums

$$S_{n_K} = \sum_{i=1}^{k} \xi_{ni} \ , \text{ k=1,2,... n-1 and } S^*_{nk} = \frac{S_{nk} - M_{nk}}{B_n}, \text{ where}$$

$$M_{nk} = ES_{nk}, \ B^2_{nk} = DS_{nk}, \ B^2_n = B^2_{nk_n}.$$

In terms of the introduced quantities, the distribution ν will be written as

$$P(\nu > k) = P(S_{n1} < S_{n2} < m+1, \ldots, S_{nk+1} < m+k). \tag{3.5}$$

If we now introduce a continuous random polyline $\xi_n(t)$ with vertices at points (t_{nk}, S^*_{nk}) and I determine the broken line $g_n(t)$ with vertices at points

$$(t_{nk}, \frac{m+k-1-M_{nk}}{B_n}), k = 1, 2, \ldots, k_n, \text{ where } t_{nk} = \frac{B^2_{nk}}{B^2_n}$$

then (3.5) can be rewritten as

$$P(\nu > k_n) = P(\xi_n(t) < g_n(t), 0 \leq t \leq 1). \tag{3.6}$$

Relation (3.6) serves as the basis for obtaining limiting distributions using the invariance principle,whereby $f(\xi_n(t)) \Longrightarrow f(w(t))$ for any continuous in C [0,1] functional f, where w (t) is a standard Wiener process (see, for example, [16]).To substantiate the applicability of the invariance principle, it is necessary to study the asymptotics of the moments and check Linderberg's condition.

Based on (3.2) and (3.3), it is easy to establish that

$$m_{ni} \equiv E\xi_{ni} = \frac{\theta_1 + \theta_2}{\theta_2 + \left(1 - \frac{i-1}{n}\right)^a} \ ,$$

$$\sigma^2_{ni} \equiv D\xi_{ni} = \frac{\theta_1^2}{\left(\theta_2 + \left(1 - \frac{i-1}{n}\right)^a\right)^2} + \frac{\theta_1}{\theta_2 + \left(1 - \frac{i-1}{n}\right)^a} + \frac{\theta_1 \left(1 - \frac{i-1}{n}\right)^a}{\left(\theta_2 + \left(1 - \frac{i-1}{n}\right)^a\right)^2} \ .$$

Asymptotics of quantities m_{nk} and B^2_{nk} with the help of the following lemma, the proof of which is not difficult.

Lemma.

If $h(x) \geq 0$ and does not increase at $[0,1]$, then for any $\alpha \in (0,1]$ and $k_n < n$

$$\sum_{k=0}^{k_n} h(1-\alpha\frac{k}{n}) = \frac{n}{\alpha}\int\limits_{1-\frac{\alpha k_n}{n}}^{1} h(x)dx + R_n,$$

where

$$1 \leq R_n \leq h(1-\alpha\frac{k}{n}) \ .$$

From this it is not difficult to obtain that if $k \leq n(1-\delta), 0 < \delta < 1$,then

$$M_{nk+1} = -\frac{n}{a}(\theta_1+\theta_2)ln\left(1-\frac{ka}{n(1+\theta_2)}\right) + \frac{\theta_1+\theta_2}{1+\theta_2}R_{n_1}, \tag{3.7}$$

$$B^2_{nk+1} = \frac{k\theta_1^2}{(1+\theta_2)^2}\frac{1}{1-\frac{ka}{(1+\theta_2)n}} + \theta_1^2 R_{n_2}, \tag{3.8}$$

where

$$1 \leq R_{n_1} \leq \frac{1+\theta_2}{\theta_2+\delta} \ , \ 1 \leq R_{n_2} \leq \frac{(1+\theta_2)^2}{(\theta_2+\delta)^2} \ .$$

The sum of the third points can be estimated in a similar way.Using these results, it is easy to estimate the Lyapunov fraction.For $k_n \to \infty$ and $k_n \leq (1-\delta)n$:

$$L_{3n} \equiv \frac{1}{B_n^3}\sum_{i=1}^{k_n} M \mid \xi_{n_i} - m_{n_i} \mid^3 = O\left(\frac{1}{\sqrt{k_n}}\right).$$

Note also that for $k \to \infty$ and $k = o(n)$:

$$M_{nk+1} = \frac{(\theta_1+\theta_2)\,k}{1+\theta_2} + \frac{ak\,(k+1)}{2(1+\theta_2)^2 n} + O\left(\frac{k^3}{n^2}\right), \tag{3.9}$$

$$B^2_{nk+1} \sim \sigma^2(n)k \ , \ \sigma^2(n) = \left(\frac{\theta_1}{1+\theta_2}\right)^2 + \frac{\theta_1}{1+\theta_2} + \frac{\theta_2}{(1+\theta_2)^2} \ . \tag{3.10}$$

4. Proofs of the main statements

Proof of the theorem 1 Under the conditions of this theorem $k_n = o(n)$ therefore, from (3.9) and (3.10) we have that $t_{nk} \sim \frac{k}{k_n}$ and

$$g_n(t_{nk}) = \frac{m + k - \frac{\theta_1+\theta_2}{1+\theta_2}k - \frac{\theta_1+\theta_2}{(1+\theta_2)^2}\frac{ak(k+1)}{2n} + O(k^3/n^2)}{\sigma(n)\sqrt{k_n}}$$

By choosing $k_n = (1+\theta_2)m^2x/2$ and noticing that $\sigma^2(n) \sim \frac{2}{1+\theta_{20}}$, we have

$$g_n(t_{n_k}) = \frac{1}{\sqrt{x}} + \frac{(1-\theta_1)m\sqrt{x}}{\sqrt{2}\sqrt{1+\theta_2}}t_{n_k} - \frac{(\theta_1+\theta_2)\,a}{\sqrt{a}\,(1+\theta_2)^{\frac{5}{2}}\,n}m^3x^{\frac{3}{2}}t_{nk}^2 + O\left(\frac{1}{m}\right).$$

Now if $k \sim k_n t, 0 < t < 1$, then

$$g_n(t) = \lim_{n\to\infty} g_n(t_{n_k}) = \frac{1}{\sqrt{x}} + \frac{\beta_0\sqrt{x/2}}{\sqrt{1+\theta_2}}t - \frac{(\theta_1+\theta_2)a\gamma_0}{4(1+\theta_2)^{\frac{5}{2}}}(x)^{3/2}t^2.$$

Thus, by virtue of the invariance principle

$$P(\nu_n > k_n) \Longrightarrow P(w(t) < g(t), 0 \le t \le 1).$$

Corollary 1 follows from the explicit representation of the following probability

$$P(w(t) < b + kt, 0 \le t \le T) = 1 - e^{-b(k+|k|)} \int_0^{Tk^2/2} p_{bk}(u)du,$$

where $p_{bk}(u) = \dfrac{b \mid k \mid e^{b|k|}}{2\sqrt{\pi}} u^{-3/2} e^{-u-b^2k^2/4u}$-Wald distribution density.

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