TWO TYPES OF INFECTIVES AMONG HOMOGENEOUS IVDU SUSCEPTIBLES

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This paper extends some classical random allocation models for intravenous drug users (IVDUs) to the case where the infectives may be of different types while the susceptibles are homogeneous. A general recursive equation for the probability generating function of the process is derived when there are only two infective types, and the first few pgfs obtained explicitly. Recursive equations for the expectations of new infectives of the two types are found, and a procedure for deriving these explicitly outlined. A simple example is provided, illustrating the difference between this case and that where both susceptibles and infectives are homogeneous.

1. Introduction

Some years ago, Gani (1991, 1993) applied a random allocation model to the problem of needle sharing among IVDUs; in this problem, both susceptibles and infectives were assumed to be homogeneous. The model was later used by Gani and Yakowitz (1993) to describe the spread of HIV among IVDUs. In a more recent paper, Gani (2002) has extended the model to the case where susceptibles are heterogeneous while infectives are homogeneous, and derived the expectations of the numbers of new infectives of different types generated after an exchange of needles. Some asymptotic results for these were also obtained.

The present paper is concerned with the case where the susceptibles are homogeneous, but the infectives may be heterogeneous, and in particular where they are of two types. Before we discuss this model, however, we remind the reader of some results for the simple case where there are n susceptibles and i infectives, both homogeneous. We shall assume that, after an exchange of needles, all susceptibles receiving needles from one or more infectives become newly infected. If there are s of these, then we may write their probability as

$$\mathbf{p}_s(i,n) = P\{s \text{ new infectives} \mid i \text{ infectives and } n \text{ susceptibles initially}\},$$

which satisfies the recursive equation

$$(1.1) \qquad \mathbf{p}_s(i+1,n) = \mathbf{p}_{s-1}(i,n)\left(1-\frac{s-1}{n}\right) + \mathbf{p}_s(i,n)\frac{s}{n}$$

Keywords and phrases: infective; susceptible; needle sharing; random allocation model.
AMS subject classifications: 60G30, 92C60.

where $1 \leq s \leq \min(i,n)$. This states that if the number of initial infectives is increased from i to $i+1$, then the probability of s new infectives either remains the same with probability s/n, or increases from $s-1$ to s with probability $1-(s-1)/n$. The probability generating function (pgf) of the $\mathbf{p}_s(i,n)$, namely

$$\phi_{i,n}(u) = \sum_{s=1}^{\min(i,n)} \mathbf{p}_s(i,n)u^s, \quad 0 \leq u \leq 1,$$

is known to satisfy the difference-differential equation

$$\phi_{i+1,n}(u) = \frac{u(1-u)}{n}\frac{d}{du}\phi_{i,n} + u\phi_{i,n}. \tag{1.2}$$

When the pgf is expressed in the form

$$\begin{aligned}\phi_{i+1,n}(u) = u^{i+1}\left[\left(1-\frac{1}{n}\right)\cdots\left(1-\frac{i}{n}\right)\right] + \cdots \\ + \frac{u^r}{n^{i+1-r}}a_r(i+1)\left[\left(1-\frac{1}{n}\right)\cdots\left(1-\frac{r-1}{n}\right)\right] + \cdots + \frac{u}{n^i}, \\ 1 < r < i,\end{aligned} \tag{1.3}$$

the coefficients $a_r(i+1)$ of u^r are found to satisfy the following relations:

$$\begin{aligned} a_{i+1}(i+1) &= a_1(i+1) = 1 \\ a_r(i+1) &= ra_r(i) + a_{r-1}(i), \quad r = 1,2,\ldots,i+1. \end{aligned}$$

These can be readily obtained by matrix methods as in Gani (2002), and lead to the following expressions for the first six values of $i = 1,2,\ldots,6$. While we assume here that $n > i$, the expression (1.2) holds equally well for $n \leq i$, with the coefficients of u^r and higher powers becoming equal to zero if $n = r-1 \leq i$.

$$\begin{array}{lllll} a_1(1) = 1, & & & & \\ a_2(2) = 1, & a_1(2) = 1, & & & \\ a_3(3) = 1, & a_2(3) = 3, & a_1(3) = 1, & & \\ a_4(4) = 1, & a_3(4) = 6, & a_2(4) = 7, & a_1(4) = 1, & \\ a_5(5) = 1, & a_4(5) = 10, & a_3(5) = 25, & a_2(5) = 15, & a_1(5) = 1, \\ a_6(6) = 1, & a_5(6) = 15, & a_4(6) = 65, & a_3(6) = 90, & a_2(6) = 31, \\ a_1(6) = 1. & & & & \end{array} \tag{1.4}$$

It should be pointed out that Woodbury (1949) and Rutherford (1954) have given alternative derivations of the formula for $\mathbf{p}_s(i,n)$, satisfying the equation (1.1); this equation also arises in certain urn models.

2. Two types of infectives

Suppose we now have two types of infectives numbering i_1 and i_2 respectively, and these share needles with n homogeneous susceptibles. We can, for example, imagine two variants of an infective virus, where type 1 is virulent while type 2 is benign; if a susceptible first exchanges needles with a type 1 (2) infective, it will become a new type 1 (2) infective, and will not succumb to the alternative type 2 (1) infection from any subsequent needle exchange. Clearly, the order in which exchanges occur is important in this situation. Let s_1 be the number of susceptibles first infected by type 1 infectives, while s_2 is the number first infected by type 2 infectives. We can then write the probability

$$\text{(2.1)}\quad \mathbf{p}_{s_1 s_2}(i_1, i_2; n) = P\{s_1,\ s_2 \text{ new infectives of types 1, 2} \mid i_1,\ i_2 \text{ infectives and } n \text{ susceptibles initially}\},$$

with $\mathbf{p}_{00}(0,0;n) = 1$, and pgf $\phi_{i_1,i_2;n}(u,v)$.

If either i_1 or i_2 is zero, the situation is reduced to that of a single type of infective as outlined in Section 1, and the relevant pgfs of the probabilities $\mathbf{p}_{s_1 0}(i_1, 0; n)$ and $\mathbf{p}_{0 s_2}(0, i_2; n)$ respectively will satisfy the difference-differential equations

$$\text{(2.2)}\quad \begin{aligned} \phi_{i_1,0}(u,v) &= \frac{u(1-u)}{n}\frac{\partial}{\partial u}\phi_{i_1-1,0} + u\phi_{i_1-1,0}(u,v), \\ \phi_{0,i_2}(u,v) &= \frac{v(1-v)}{n}\frac{\partial}{\partial v}\phi_{0,i_2-1} + v\,\phi_{0,i_2-1}(u,v), \end{aligned}$$

where, for simplicity, we have omitted the initial number of susceptibles n in $\phi_{i_1,i_2;n}(u,v)$. The solutions of the equations (2.2) are of the form (1.3) with v replacing u in the second case.

When both i_1 and i_2 are non-zero, then assuming that an extra infective of type 1 is added with probability $p > 0$, while one of type 2 is added with probability $q = 1 - p > 0$, the probabilities (2.1) can be seen to satisfy the recurrence relation

$$\text{(2.3)}\quad \begin{aligned} &\mathbf{p}_{s_1 s_2}(i_1, i_2; n) \\ &= [p\,\mathbf{p}_{s_1 s_2}(i_1 - 1, i_2; n) + q\,\mathbf{p}_{s_1 s_2}(i_1, i_2 - 1; n)]\left[\frac{s_1 + s_2}{n}\right] \\ &\quad + [p\,\mathbf{p}_{s_1 - 1\, s_2}(i_1 - 1, i_2; n) + q\,\mathbf{p}_{s_1 s_2 - 1}(i_1, i_2 - 1; n)]\left[1 - \frac{s_1 + s_2 - 1}{n}\right] \end{aligned}$$

for all $1 \le s_1 \le \min(i_1, n)$, $1 \le s_2 \le \min(i_2, n)$. Multiplying (2.3) by $u^{s_1}v^{s_2}$ for all permissible values of s_1, s_2 , we find that

$$\begin{aligned}(2.4)\quad \phi_{i_1,i_2}(u,v) = {}& \frac{p(1-u)}{n}\left[u\frac{\partial}{\partial u}\phi_{i_1-1,i_2} + v\frac{\partial}{\partial v}\phi_{i_1-1,i_2}\right] + pu\,\phi_{i_1-1,i_2} \\ &+ \frac{q(1-v)}{n}\left[u\frac{\partial}{\partial u}\phi_{i_1,i_2-1} + v\frac{\partial}{\partial v}\phi_{i_1,i_2-1}\right] + qv\,\phi_{i_1,i_2-1}.\end{aligned}$$

Thus, starting from $\phi_{0,0}(u,v) = 1$, and the first few results obtained from (2.2), namely

$$(2.5)\qquad \begin{aligned} &\phi_{1,0}(u,v) = u && \phi_{0,1}(u,v) = v \\ &\phi_{2,0}(u,v) = \frac{u}{n} + u\left(1-\frac{1}{n}\right) && \phi_{0,2}(u,v) = \frac{v}{n} + v\left(1-\frac{1}{n}\right),\end{aligned}$$

we can, using (2.4), obtain the pgfs

$$\begin{aligned}\phi_{1,2}(u,v) &= \frac{1}{n}[uq^2 + v(1-q^2)] + \frac{1}{n}\left(1-\frac{1}{n}\right)[uv(p+2q+q^2) + pv^2(q+2)] \\ &\quad + \left(1-\frac{1}{n}\right)\left(1-\frac{2}{n}\right)uv^2 \\ \phi_{2,1}(u,v) &= \frac{1}{n}[vp^2 + u(1-p^2)] + \frac{1}{n}\left(1-\frac{1}{n}\right)[uv(q+2p+p^2) + qu^2(p+2)] \\ (2.6)\qquad &\quad + \left(1-\frac{1}{n}\right)\left(1-\frac{2}{n}\right)u^2v \\ \phi_{2,2}(u,v) &= \frac{1}{n^3}[u(pq^2+q-p^2q) + v(qp^2+p-pq^2)] \\ &\quad + \frac{1}{n^2}\left(1-\frac{1}{n}\right)[u^2(3pq^2+4q^2) + uv(1+9pq+2p^2+2q^2) \\ &\qquad\qquad + v^2(3p^2q+4p^2)] \\ &\quad + \frac{1}{n}\left(1-\frac{1}{n}\right)\left(1-\frac{2}{n}\right)[uv^2(2p^2+2p^2q+3p+2pq+q^2) \\ &\qquad\qquad + u^2v(2pq^2+2q^2+3q+p^2+2pq)] \\ &\quad + \left(1-\frac{1}{n}\right)\left(1-\frac{2}{n}\right)\left(1-\frac{3}{n}\right)u^2v^2.\end{aligned}$$

Note that when we set $u = v = 1$ in the $\phi_{i_1,i_2}(u,v)$, we find that the coefficients are precisely those described in (1.4); for example, when $i_1 = i_2 = 2$, so that $i = i_1 + i_2 = 4$, the coefficients for the last pgf in (2.6) reduce to 1, 6, 7, 1, as in $a_4(4)$, $a_3(4)$, $a_2(4)$ and $a_1(4)$ of (1.4).

3. Expectations

We shall now assume that there are always n initial susceptibles, and remove this suffix from our notation. It was established in Gani (2002) that for i

initial infectives of a single type, the expectation of the number of new infectives Y_i after an exchange of needles was

$$m(i) = E(Y_i) = n\big(1 - (1 - 1/n)^i\big). \tag{3.1}$$

Thus, in the case of two types of infectives, with $i_1 = j$, $i_2 = k$, we have when $k = 0$, and $j = 0$ respectively, the expectations

$$\begin{aligned} m_1(j,0) &= E(Y_{1;j0}) = n\big(1 - (1 - 1/n)^j\big), \\ m_2(0,k) &= E(Y_{2;0k}) = n\big(1 - (1 - 1/n)^k\big). \end{aligned} \tag{3.2}$$

When j and k are both positive, the situation becomes more complicated. If we differentiate (2.4) with respect to u, we find, recalling that $i_1 = j$ and $i_2 = k$,

$$\begin{aligned} \frac{\partial}{\partial u}\phi_{jk} &= -\left[u\frac{\partial}{\partial u}\phi_{j-1\,k} + v\frac{\partial}{\partial v}\phi_{j-1\,k}\right]\frac{p}{n} \\ &+ \left[\frac{\partial}{\partial u}\phi_{j-1\,k} + u\frac{\partial^2}{\partial u^2}\phi_{j-1\,k} + v\frac{\partial^2}{\partial u \partial v}\phi_{j-1\,k}\right]\frac{p(1-u)}{n} + p\,\phi_{j-1\,k} + pu\frac{\partial}{\partial u}\phi_{j-1\,k} \\ &+ \left[\frac{\partial}{\partial u}\phi_{jk-1} + u\frac{\partial^2}{\partial u^2}\phi_{jk-1} + v\frac{\partial^2}{\partial u \partial v}\phi_{jk-1}\right]\frac{q(1-v)}{n} + qv\frac{\partial}{\partial u}\phi_{j\,k-1}. \end{aligned} \tag{3.3}$$

Setting $u = v = 1$, we obtain the relation

$$\begin{aligned} m_1(j,k) &= E(Y_{1;jk}) \\ &= m_1(j-1,k)p\left(1 - \frac{1}{n}\right) - m_2(j-1,k)\frac{p}{n} + qm_1(j,k-1) + p, \end{aligned} \tag{3.4}$$

and similarly on differentiating (2.4) with respect to v and setting $u = v = 1$,

$$\begin{aligned} m_2(j,k) &= E(Y_{2;jk}) \\ &= m_2(j,k-1)q\left(1 - \frac{1}{n}\right) - m_1(j,k-1)\frac{q}{n} + pm_2(j-1,k) + q. \end{aligned} \tag{3.5}$$

Writing these in matrix form, we note that

$$
(3.6)\quad
\begin{bmatrix}
m_1(j,k) \\
m_2(j,k) \\
m_1(j+1,k-1) \\
m_2(j+1,k-1) \\
\vdots \\
m_1(j+k-1,1) \\
m_2(j+k-1,1) \\
m_1(j+k,0) \\
1
\end{bmatrix}
$$

$$
=\begin{bmatrix}
p(1-\frac{1}{n}) & -\frac{p}{n} & q & 0 & 0 & 0 & \cdots & p \\
0 & p & -\frac{q}{n} & q(1-\frac{1}{n}) & 0 & 0 & \cdots & q \\
0 & 0 & p(1-\frac{1}{n}) & -\frac{p}{n} & q & 0 & \cdots & p \\
0 & 0 & 0 & p & -\frac{q}{n} & q(1-\frac{1}{n}) & \cdots & q \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\
0 & \cdots & 0 & 0 & p(1-\frac{1}{n}) & -\frac{p}{n} & q & p \\
0 & \cdots & 0 & 0 & 0 & p & -\frac{q}{n} & q \\
0 & \cdots & 0 & 0 & 0 & 0 & (1-\frac{1}{n}) & 1 \\
0 & \cdots & 0 & 0 & 0 & 0 & 0 & 1
\end{bmatrix}
\begin{bmatrix}
m_1(j-1,k) \\
m_2(j-1,k) \\
m_1(j,k-1) \\
m_2(j,k-1) \\
\vdots \\
m_1(j+k-2,1) \\
m_2(j+k-2,1) \\
m_1(j+k-1,0) \\
1
\end{bmatrix},
$$

where it is assumed that $m_1(j,i_2)$, $m_2(j,i_2)$ are known for all values of $i_2 < k-1$. Thus, one can obtain these expectations for increasing j recursively. A simple example will illustrate our proposed procedure.

We know the values of $m_1(j,0)$ and $m_2(j,0)$ from (3.2). Let us now derive the $m_1(j,1)$ and $m_2(j,1)$ using (3.6), or

$$
\begin{bmatrix}
m_1(j,1) \\
m_2(j,1) \\
m_1(j+1,0) \\
1
\end{bmatrix}
=\begin{bmatrix}
p(1-\frac{1}{n}) & -\frac{p}{n} & q & p \\
0 & p & -\frac{q}{n} & q \\
0 & 0 & (1-\frac{1}{n}) & 1 \\
0 & 0 & 0 & 1
\end{bmatrix}
\begin{bmatrix}
m_1(j-1,1) \\
m_2(j-1,1) \\
m_1(j,0) \\
1
\end{bmatrix}.
$$

If we set $j=1$ for the right hand vector, then $m_1(0,1)=0$, $m_2(0,1)=1$, $m_2(1,0)=1$, so that

$$
(3.7)\quad
\begin{bmatrix}
m_1(j,1) \\
m_2(j,1) \\
m_1(j+1,0) \\
1
\end{bmatrix}
=\begin{bmatrix}
p(1-\frac{1}{n}) & -\frac{p}{n} & q & p \\
0 & p & -\frac{q}{n} & q \\
0 & 0 & (1-\frac{1}{n}) & 1 \\
0 & 0 & 0 & 1
\end{bmatrix}^{j}
\begin{bmatrix}
0 \\
1 \\
1 \\
1
\end{bmatrix}.
$$

Using the canonical form of the matrix in (3.7), we find that

$$
\text{(3.8)}\qquad \begin{bmatrix} m_1(j,1) \\ m_2(j,1) \\ m_1(j+1,0) \\ 1 \end{bmatrix} = \begin{bmatrix} 1 & -1 & \frac{p-nq}{q} & n \\ 0 & 1 & 1 & 0 \\ 0 & 0 & \frac{1-nq}{q} & n \\ 0 & 0 & 0 & 1 \end{bmatrix}
$$
$$
\times \begin{bmatrix} [p(1-\frac{1}{n})]^j & 0 & 0 & 0 \\ 0 & p^j & 0 & 0 \\ 0 & 0 & (1-\frac{1}{n})^j & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} 1 & 1 & -1 & 0 \\ 0 & 1 & -\frac{q}{1-nq} & \frac{nq}{1-nq} \\ 0 & 0 & \frac{q}{1-nq} & -\frac{nq}{1-nq} \\ 0 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} 0 \\ 1 \\ 1 \\ 1 \end{bmatrix}.
$$

Hence, we obtain the expectations

$$
\text{(3.9)}\qquad \begin{aligned} m_1(j,1) &= n\left[1 - \frac{(nq-p)(1-1/n)^{j+1}}{nq-1}\right] + \frac{p^{j+1}}{nq-1} \\ m_2(j,1) &= \frac{nq(1-1/n)^{j+1} - p^{j+1}}{nq-1}, \\ m_1(j+1,0) &= n\left[1 - \left(1-\frac{1}{n}\right)^{j+1}\right]. \end{aligned}
$$

We can now proceed to obtain all $m_1(j,2)$, $m_2(j,2)$, and then $m_1(j,k)$, $m_2(j,k)$ similarly, although the relevant recursion matrices will be more complicated in this case. We note that

$$
m_1(j,k) + m_2(j,k) = n\left[1 - \left(1-\frac{1}{n}\right)^{j+k}\right] = m(j+k),
$$

where $m(j+k)$ is the total expected number of new infections due to the $j+k$ initial infectives. Hence, if all $m_1(j,k)$ are known, so also will all $m_2(j,k)$.

An asymptotic result which follows from (3.9) is that if j and n are both large with $j = cn - 1$, where c is some constant, then

$$
\text{(3.10)}\qquad \begin{aligned} m_1(cn-1,1) &\to n\left[1 - \frac{(nq-p)e^{-c}}{(nq-1)}\right] + \frac{p^{cn}}{nq-1} \to n(1-e^{-c}), \\ m_2(cn-1,1) &\to \frac{nqe^{-c} - p^{cn}}{nq-1} \to e^{-c}. \end{aligned}
$$

Even a small value of k, such as $k = 1$ makes a difference to the number of new type 1 infectives after a single needle exchange. Let the j type 1 initial infectives be virulent, while the single type 2 initial infective is benign. Then for $p = q = 0.5$, $n = 10$, and $j = 1, 5, 10$, the Table below gives the expected number of new infectives of type 1, as against the number of all new infectives $m(j+1)$ when the $j+1$ initial infectives are homogeneous.

Table 1. Expected new infectives for $n = 10$

	$m_1(j,1)$	$m(j+1)$
$j = 1$	0.95	1
$j = 5$	4.026	4.685
$j = 10$	6.480	6.862

4. Concluding remarks

The random allocation model for the spread of HIV among IVDUs can lead to fairly complicated equations when there are two types of initial infectives. We have considered the partial differential equation governing the pgf of the process, and shown how it can be used to derive the pgf recursively. Equations for the expectations of the numbers of new type 1 and type 2 infectives were obtained, and again led to recursive equations. The case of $j > 0$ type 1 and 1 type 2 initial infectives is solved explicitly, and the procedure for $k > 1$ type 2 infectives outlined. Finally, an example for the expectation $m_1(j,1)$ when there are $n = 10$ initial susceptibles is given; the existence of even a single type 2 initial infective appears to decrease the new type 1 infectives.

An important problem remaining to be solved is the case where there exist two types of initial infectives and two types of susceptibles with different susceptibilities as, for example, with adults and children. Further research on this topic is in progress.

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