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A stochastic model for expected time to seroconversion under correlated intercontact times using SCBZ property

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Abstract

This paper focuses on the study of a stochastic model for predicting seroconversion time of HIV transmission under correlated intercontact times. In the estimation of expected time to seroconversion, there is an important role for the interarrival times between successive contacts and it has a significant influence. We propose a stochastic model assuming the intercontact times between successive contacts are correlated random variables and the threshold distribution is SCBZ property. The expected time to seroconversion and its variance are derived and numerical illustrations are provided.

Key words: Acquired Immuno Deficiency Syndrome, Antigenic Diversity Threshold, Human Immunodeficiency Virus, Intercontact times, Seroconversion.

Notations :

X_i : a random variable denoting the increase in the antigenic diversity arising due to the HIV transmitted during the i^{th} contact $X_1, X_2, \ldots, X_k$ are continuous i.i.d. random variables with p.d.f. g(.) and c.d.f. G(.).

Y : a continuous random variable denoting the threshold level having SCBZ property.

U_i : a continuous random variable denoting the interarrival times between successive contacts with p.d.f *f*(.) and c.d.f F(.).

$g_k(.)$: the p.d.f of random variable $\sum_{i=1}^{k} X_i$.

$F_k(.)$: the convolution of F(.).

T : a continuous random variable denoting the time to seroconversion with p.d.f. *l*(.) and c.d.f. L(.).

$V_k(t)$: the probability of exactly k contacts in (o, t].

*l**(s) : the Laplace transform of *l*(t).

f *(s): the Laplace transform of *f*(t).

ρ : the correlation between Xi and Xj, i j.

Z_k : $\sum_{i=1}^{k} U_i$

Introduction

The incident and spread of Human Immuno–deficiency Virus (HIV) infection and consequent Acquired Immuno Deficiency Syndrome (AIDS) as created pandemic situation in the world all over. The intensity of occurrence and spread is highly pronounced in many countries with the result that the individual as well as the government have to meet a great burden of financial stressed in treating for the infection and its consequences. The transmission of HIV is possible through homo or heterosexual contacts, blood transfusion, use of unsterile needles and mother to fetus. The per contact transmission probability is known as infectivity. Jewell and Shiboski[3] have obtained the expression for hazard rate and prevalence function using the available data from the partner studies.

The time to seroconversion from the point of infection depends upon what is known as antigenic diversity which acts against the immune ability of an individual. Every individual has a threshold level of antigenic diversity. If the antigenic diversity due to acquiring more and more of HIV infection due to homo or heterosexual contacts exceeds the threshold level, then the immune system of the human body is completely suppressed which in turn leads to seroconversion. For a detailed study of antigenic threshold and its estimation one can refer to Nowak and May[4] and Stilianakis *et al.*[6].

A stochastic model based on the cumulative damage process is derived and using this model it is possible to obtain the expected time to seroconversion and its variance. The antigenic diversity level which induces the seroconversion is known as the random antigenic diversity threshold. Every contact induces and contributes to the antigenic diversity which when crosses the threshold level will result in the seroconversion of an individual. Every contact is depicted as a shock and in every contact there is some contribution to antigenic diversity which in other words is the damage to the immune capacity of an individual. Cumulative damage process and shock model are widely known in reliability theory. A detailed account of the same could be seen in Esary *et al.*[1]. In the derivation of present model the concepts of cumulative damage process and shock model are taken as basis. In developing such a model the basic assumption made was that the intercontact timings between successive contacts are i.i.d random variables.

In this paper a stochastic model assumes that the intercontact timings between successive contacts are correlated random variables and the threshold distribution which follows SCBZ property. The assumption of correlated intercontact timings seems plausible by the fact that any partner after every contact with an index may have a physiological obsession and fear of contracting the disease, which may have an impact on intercontact times of contacts such as prolongation of intercontact times. Shock model with correlated intercontact times has been studied by Sathiyamoorthi[5]. In developing this model the result of Gurland[2] has been used. Using the same concept, time to seroconversion and its variance are obtained

in this paper. In this study the theoretical results are substantiated using numerical data simulated.

Assumptions of the model :

- Sexual contact is the only source of HIV transmission.
- When an uninfected individual has sexual contact with a HIV infected partner, a random number of HIV gets transmitted.
- An individual is exposed to a damage acting on the immune system and damage is assumed to be linear and cumulative.
- The intercontact timings between successive contacts are not independent but are correlated.
- The total damage caused when exceeds a threshold level Y which itself a random variable, the seroconversion occurs and a person is recognized as seropositive.
- The process which generates the contacts, the sequence of damages and threshold are mutually independent.

Results

Let Y have the SCBZ property

$$H(y)=\begin{cases}1-e^{-\theta_1 y} & ;y\le\tau_0\\ 1-e^{-\theta_1\tau_0}e^{-\theta_2(y-\tau_0)} & ;\tau_0<y\end{cases}$$

for a fixed $\tau = \tau_0$.

Assuming the truncation level itself a random variable such that τ follows exponential with parameter λ, we have

$$\therefore H(y)=1-\frac{\theta_1-\theta_2}{\lambda+\theta_1-\theta_2}e^{-(\theta_1+\lambda)y}-\frac{\lambda}{\lambda+\theta_1-\theta_2}e^{-\theta_2 y}$$

Now

$$h(y)=\frac{d}{dy}[H(y)]$$

$$=\frac{\theta_1-\theta_2}{\lambda+\theta_1-\theta_2}(\theta_1+\lambda)e^{-(\theta_1+\lambda)y}+\frac{\theta_2\lambda}{\lambda+\theta_1-\theta_2}e^{-\theta_2 y}$$

$$\therefore h(y)=p(\theta_1+\lambda)\ e^{-(\theta_1+\lambda)y}+q\theta_2\ e^{-\theta_2 y}$$

Where

$$p=\frac{\theta_1-\theta_2}{\lambda+\theta_1-\theta_2},\ q=\frac{\lambda}{\lambda+\theta_1-\theta_2}\ \text{and}\ p+q=1$$

Now, $P[X_1+X_2+\cdots+X_k<Y]=$

$$\int_0^\infty g_k(x)\ [1-H(x)]dx$$

$$=\int_0^\infty g_k(x)\ [p\,e^{-(\theta_1+\lambda)x}+q\,e^{-\theta_2 x}]dx$$

$$=p\int_0^\infty g_k(x)\ e^{-(\theta_1+\lambda)x}dx+q\int_0^\infty g_k(x)\ e^{-\theta_2 x}\ dx$$

$$=p\,g_k^*(\theta_1+\lambda)+q\,g_k^*(\theta_2)$$

$$=p[g^*(\theta_1+\lambda)]^k+q[g^*(\theta_2)]^k$$

S(t) = P [T > t]

$$=\sum_{k=0}^\infty V_k(t)P[X_1+X_2+\cdots+X_k<Y]$$

$$=\sum_{k=0}^\infty[F_k(t)-F_{k+1}(t)]\ \ [p[g^*(\theta_1+\lambda)]^k+q[g^*(\theta_2)]^k]$$

$$=p\sum_{k=0}^\infty[F_k(t)-F_{k+1}(t)]\ \ [g^*(\theta_1+\lambda)]^k$$

$$+q\sum_{k=0}^\infty[F_k(t)-F_{k+1}(t)][g^*(\theta_2)]^k$$

$$L(t)=1-S(t)$$

$$= p\left[1 - g^*(\theta_1 + \lambda)\right] \sum_{k=1}^{\infty}\left[g^*(\theta_1 + \lambda)\right]^{k-1} F_k(t)$$

$$+ q\left[1 - g^*(\theta_2)\right] \sum_{k=1}^{\infty}\left[g^*(\theta_2)\right]^{k-1} F_k(t)$$

On simplification

P.d.f of L(t) is given by

$$l(t) = p\left[1 - g^*(\theta_1 + \lambda)\right]\sum_{k=1}^{\infty}\left[g^*(\theta_1 + \lambda)\right]^{k-1} f_k(t)$$

$$+ q\left[1 - g^*(\theta_2)\right]\sum_{k=1}^{\infty}\left[g^*(\theta_2)\right]^{k-1} f_k(t)$$

Laplace transform of $l(t)$ is given by

$$l^*(s) = p\left[1 - g^*(\theta_1 + \lambda)\right] \sum_{k=1}^{\infty}\left[g^*(\theta_1 + \lambda)\right]^{k-1} f_k^*(s)$$

$$+ q\left[1 - g^*(\theta_2)\right] \sum_{k=1}^{\infty}\left[g^*(\theta_2)\right]^{k-1} f_k^*(s)$$

Let $U_1, U_2, \ldots, U_k$ represent the interarrival times between successive contacts which are correlated. Gurland[2] has derived the cumulative distribution function of the sum, say $Z_k = \sum_{i=1}^{k} U_i$, when U_i's from a sequence of exchangeable constantly correlated random variables each having exponential distribution with p.d.f.

$$f(u) = \mu\ e^{-u\mu}; \mu > 0,\ 0 < u < \infty$$

Such that the correlation coefficient between U_i and U_j $(i \neq j)$ is ρ.

This c.d.f is given by

$$F_k(u) = P[Z_k \leq u]$$

$$= (1 - \rho)\sum_{i=0}^{\infty} \frac{(\rho k)^i \eta[k + i, u/b]}{[1 - \rho + k\rho]^{i+1}(k + i - 1)!}$$

where

$$b = \frac{(1-\rho)}{\mu} \text{ and}$$

$$\eta(k, u) = \int_0^u e^{-\mu}\ \mu^{k-1}\ d\mu$$

The Laplace transform of the density function of Z_k is given by

$$f_k^*(s) = \frac{1}{(1+bs)^k\left[1 + \frac{k\rho\, bs}{(1-\rho)\ (1+bs)}\right]}$$

$$l^*(s) = p\left[1 - g^*(\theta_1 + \lambda)\right] \sum_{k=1}^{\infty}\left[g^*(\theta_1 + \lambda)\right]^{k-1} \frac{1}{(1+bs)^k\left[1 + \frac{k\rho\, bs}{(1-\rho)\ (1+bs)}\right]}$$

$$+ q\left[1 - g^*(\theta_2)\right] \sum_{k=1}^{\infty}\left[g^*(\theta_2)\right]^{k-1} \frac{1}{(1+bs)^k\left[1 + \frac{k\rho\, bs}{(1-\rho)\ (1+bs)}\right]} \quad (1)$$

Where

$$f_k^*(s) = \frac{1}{(1+bs)^k\left[1 + \frac{k\rho\, bs}{(1-\rho)\ (1+bs)}\right]}$$

$$= (1+bs)^{1-k}\left[1+bs+\frac{k\rho s}{\mu}\right]^{-1}$$ On simplification

$$\frac{df_k^*(s)}{ds} = (1+bs)^{1-k}(-1)\left[1+bs+\frac{k\rho s}{\mu}\right]^{-2}\left[b+\frac{k\rho}{\mu}\right]+\left[1+bs+\frac{k\rho s}{\mu}\right]^{-1}(1-k)\ (1+bs)^{-k}b$$

$$= -\ (1+bs)^{1-k}\left[1+bs+\frac{k\rho s}{\mu}\right]^{-2}\left[b+\frac{k\rho}{\mu}\right]+b(1-k)\ (1+bs)^{-k}\left[1+bs+\frac{k\rho s}{\mu}\right]^{-1}$$

$$f^{*\prime}(0) = \left.\frac{df_k^*(s)}{ds}\right|_{s=0} = -\ \left[b+\frac{k\rho}{\mu}\right]+b(1-k)$$

$$= \left(\frac{-k}{\mu}\right)$$ On simplification (2)

$$f^{*\prime\prime}(0) = \left.\frac{d^2 f_k^*(s)}{ds^2}\right|_{s=0} = -\ (1-k)b\left[b+\frac{k\rho}{\mu}\right]+2\left[b+\frac{k\rho}{\mu}\right]^2 - b^2\ k(1-k)-b(1-k)\ \left[b+\frac{k\rho}{\mu}\right]$$

$$= \frac{k(1-\rho^2)+k^2(1+\rho^2)}{\mu^2}$$ On simplification (3)

$$E(T) = -\left.\frac{dl^*(s)}{ds}\right|_{s=0}$$

$$= p\left[1-g^*(\theta_1+\lambda)\right]\ \sum_{k=1}^{\infty}\left[g^*(\theta_1+\lambda)\right]^{k-1} f^{*\prime}(0)+q\left[1-g^*(\theta_2)\right]\ \sum_{k=1}^{\infty}\left[g^*(\theta_2)\right]^{k-1} f^{*\prime}(0)$$ (4)

Substituting equation (2) in (4)

$$= p\left[1-g^*(\theta_1+\lambda)\right]\sum_{k=1}^{\infty}\left[g^*(\theta_1+\lambda)\right]^{k-1}\left(\frac{-k}{\mu}\right)+q\left[1-g^*(\theta_2)\right]\sum_{k=1}^{\infty}\left[g^*(\theta_2)\right]^{k-1}\left(\frac{-k}{\mu}\right)$$

Let $g^*(\theta_1+\lambda) = \frac{\alpha}{\alpha+\theta_1+\lambda}$ and $g^*(\theta_2) = \frac{\alpha}{\alpha+\theta_2}$

$$E(T) = \frac{1}{\mu(\lambda+\theta_1-\theta_2)}\left[(\theta_1-\theta_2)\left(\frac{\alpha+\theta_1+\lambda}{\theta_1+\lambda}\right)+\lambda\left(\frac{\alpha+\theta_2}{\theta_2}\right)\right]$$ On simplification (5)

$$E(T^2) = \left.\frac{d^2 l^*(s)}{ds^2}\right|_{s=0}$$

$$= p\left[1 - g^*(\theta_1+\lambda)\right] \sum_{k=1}^{\infty}\left[g^*(\theta_1+\lambda)\right]^{k-1} f_k^{*u}(0) + q\left[1 - g^*(\theta_2)\right] \sum_{k=1}^{\infty}\left[g^*(\theta_2)\right]^{k-1} f_k^{*u}(0) \quad (6)$$

Substituting equation (3) in (6)

$$= p\left[1 - \frac{\alpha}{\alpha+\theta_1+\lambda}\right]\sum_{k=1}^{\infty}\left(\frac{\alpha}{\alpha+\theta_1+\lambda}\right)^{k-1}\left(\frac{k(1-\rho^2)+k^2(1+\rho^2)}{\mu^2}\right)$$

$$+ q\left[1 - \frac{\alpha}{\alpha+\theta_2}\right] \sum_{k=1}^{\infty}\left(\frac{\alpha}{\alpha+\theta_2}\right)^{k-1}\left(\frac{k(1-\rho^2)+k^2(1+\rho^2)}{\mu^2}\right)$$

$$E(T^2) = \frac{2}{\mu^2(\lambda+\theta_1-\theta_2)}\left[\frac{(\theta_1-\theta_2)\left[1+\rho^2\left(\frac{\alpha}{\alpha+\theta_1+\lambda}\right)\right](\alpha+\theta_1+\lambda)^2}{(\theta_1+\lambda)^2}\right.$$

$$\left. + \frac{\lambda\left[1+\rho^2\left(\frac{\alpha}{\alpha+\theta_2}\right)\right](\alpha+\theta_2)^2}{\theta_2^2}\right] \text{ On simplification} \quad (7)$$

Using equations (5) and (7)

$V(T) = E(T^2) - [E(T)]^2$

$$= \frac{2}{\mu^2(\lambda+\theta_1-\theta_2)}\left[\frac{(\theta_1-\theta_2)\left[1+\rho^2\left(\frac{\alpha}{\alpha+\theta_1+\lambda}\right)\right](\alpha+\theta_1+\lambda)^2}{(\theta_1+\lambda)^2} + \frac{\lambda\left[1+\rho^2\left(\frac{\alpha}{\alpha+\theta_2}\right)\right](\alpha+\theta_2)^2}{\theta_2^2}\right]$$

$$- \left\{\frac{1}{\mu(\lambda+\theta_1-\theta_2)}\left[(\theta_1-\theta_2)\left(\frac{\alpha+\theta_1+\lambda}{\theta_1+\lambda}\right)+\lambda\left(\frac{\alpha+\theta_2}{\theta_2}\right)\right]\right\}^2$$

Numerical Illustrations

Table 1.

α	l =1, μ=1, θ_1=1.5, θ_2=0.5, ρ=0.5	
	E(T)	V(T)
0.1	1.1200	1.3376
0.2	1.2400	1.7504
0.3	1.3600	2.2384
0.4	1.4800	2.8016
0.5	1.6000	3.4400
0.6	1.7200	4.1536
0.7	1.8400	4.9424
0.8	1.9600	5.8064
0.9	2.0800	6.7456

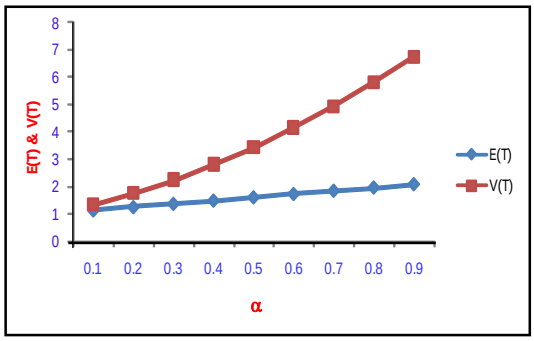

Fig. 1

The value of E(T) corresponding to the variation in α with λ, μ, θ_1, θ_2 and ρ are fixed. α happen to the parameter of the random variable depicting the amount of antigenic diversity contribution in the successive contact. If α increase, the expected time to seroconversion and variance of seroconversion are increases. This is due to fact that g(.) is the distribution of $X_1's$ the magnitude of contribution to antigenic diversity. Since $E(T)=\frac{1}{\alpha}$, as α increases there is a decrease in the contribution of antigenic diversity. Hence mean time to seroconversion is increases, so also the value of variance of seroconversion time.

Table 2.

θ_1	λ=1, μ=1, α=0.1, θ_2=0.5, ρ=0.5	
	E(T)	V(T)
1.0	1.1500	1.4213
1.5	1.1200	1.3376
2.0	1.1000	1.2817
2.5	1.0857	1.2417
3.0	1.0750	1.2116
3.5	1.0667	1.1881
4.0	1.0600	1.1694
4.5	1.0545	1.1541
5.0	1.0500	1.1413

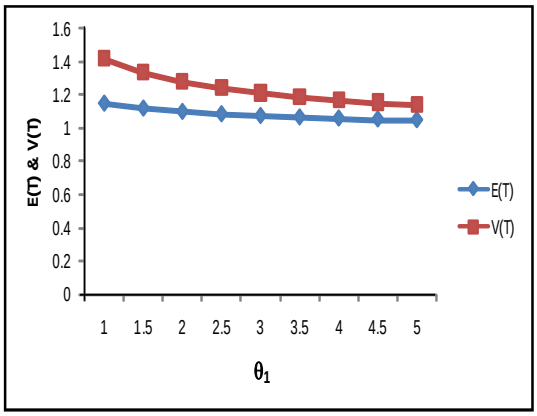

Fig. 2

It is observed from the Table 2 also the graph as the value of θ_1 is the parameter of the antigenic diversity threshold which is a random variable distributed as exponential below the truncation point τ increases the mean time to seroconversion is decreases. It is also quite reasonable as regards the variation it could be seen that as value of θ_1 increases, the variance decreases.

Table 3.

θ_2	λ=1, μ=1, α=0.1, θ_1=1.5, ρ=0.5	
	E(T)	V(T)
0.1	1.4400	2.9504
0.2	1.2400	1.8164
0.3	1.1733	1.5318
0.4	1.1400	1.4069
0.5	1.1200	1.3376
0.6	1.1067	1.2937
0.7	1.0971	1.2636
0.8	1.0900	1.2415
0.9	1.0844	1.2248

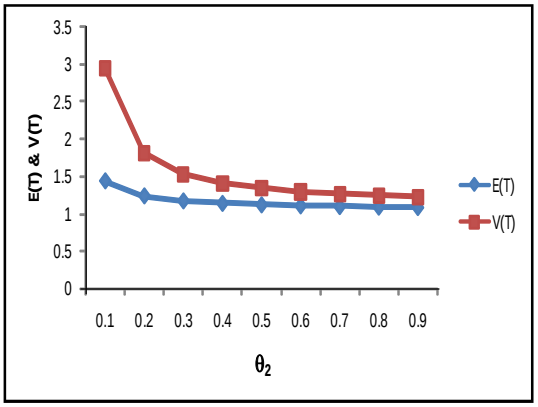

Fig. 3

From the Table 3 we observe that for fixed α, λ, μ, θ_1 and ρ when θ_2 is allowed to increase then mean time to seroconversion decreases. The same tendency is also noted on the variance of the seroconversion time of the HIV transmission.

Table 4.

λ	μ=1, α=0.1, θ_1=1.5, θ_2=0.5, ρ=0.5	
	E(T)	V(T)
1	1.1200	1.3376
2	1.1429	1.4039
3	1.1556	1.4399
4	1.1636	1.4625
5	1.1692	1.4779
6	1.1733	1.4891
7	1.1765	1.4975
8	1.1789	1.5044
9	1.1809	1.5098
10	1.1826	1.5142

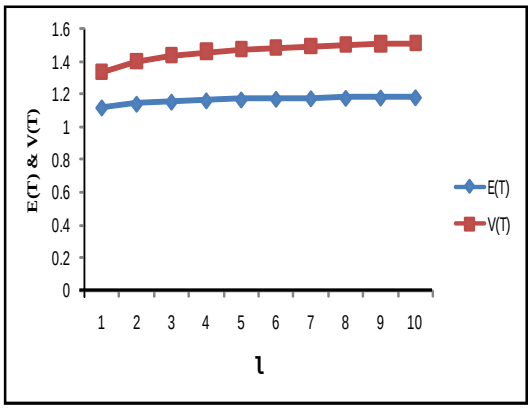

Fig. 4

If the value of λ which is the parameter of the exponential distribution of the random variable τ denoting the truncation point increases, then the expected time to seroconversion increases as indicated in Table 4, so also is the variance of T.

Table 5.

μ	λ=1, α=0.1, θ_1=1.5, θ_2=0.5, ρ=0.5	
	E(T)	V(T)
1	1.1200	1.3376
2	0.5600	0.3344
3	0.3733	0.1486
4	0.2800	0.0836
5	0.2240	0.0535
6	0.1867	0.0371
7	0.1600	0.0273
8	0.1400	0.0209
9	0.1244	0.0165
10	0.1120	0.0134

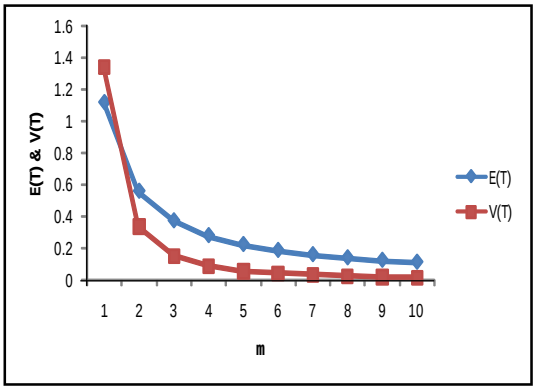

Fig. 5

In Table 5 the value of expected time to seroconversion corresponding to the variation in μ with α, λ, θ_1, θ_2 and ρ are kept fixed. If μ which is the parameter of the distribution of interarrival time which exponentially distributed is given as μ increases, the value of $\frac{1}{\mu}$ decreases that means the interarrival time between contacts become smaller and so there is corresponding decrease in expected time to seroconversion and also its variance.

Table 6.

ρ	λ=1, μ=1, α=0.1, θ_1=1.5, θ_2=0.5
	V(T)
0.1	1.2700
0.2	1.2785
0.3	1.2925
0.4	1.3123
0.5	1.3376
0.6	1.3686
0.7	1.4051
0.8	1.4474
0.9	1.4953

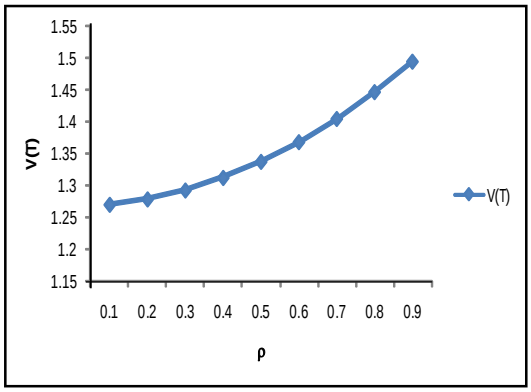

Fig. 6

When ρ which is the constant correlation between interarrival times between successive contacts increases for fixed α, λ, μ, θ_1 and θ_2, the variance of the seroconversion increases.

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