Spillover rate is not a predictor of host jump risk

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1 Abstract

Spillover of infectious diseases is a significant issue for human, animal, and plant health, in part due to their potential to host jump. Current approaches to predict and prevent host jumps are structured around discovering new viruses, drawing associations between pathogen characteristics and host jump risk, and managing spillover, but prediction and prevention are still elusive. Spillover is a critical step in the process of completing a host jump, so it is often assumed that a pathogen's spillover rate is predictive of host jump risk. However, this may not necessarily be the case. While a pathogen that spills over into a novel host frequently will indeed have many opportunities to establish itself, the lack of success establishing itself in previous spillovers demonstrates a poor ability to do so. In comparison, a pathogen that rarely spills over will have few opportunities to establish itself, but may be well suited to do so, and could, in theory, be more likely to host jump despite these limited opportunities. Here we address the question of which of these poses the greater risk. Using a Bayesian framework, we create a model to quantify the probability that a host jump occurs in some future time interval. This model only depends on the number of spillover events in the past and future, and our uncertainty regarding the probability that a single spillover will result in a host jump. We derive an analytical solution to this model, which shows that when past and future spillover rates are linearly correlated, a pathogen's inherent rate of spillover is a poor predictor of host jump risk owing to two complementary factors. First, the pathogens that pose the greatest host jump risk may be either those that spillover extremely rarely or extremely commonly, with the result depending on our prior uncertainly in the probability that a spillover will result in a host jump. Second, as spillover rate becomes large, the increase in the number of opportunities for a host jump to occur conferred by the increase in the number of spillover events is exactly balanced by a decrease in the probability of success for each individual spillover event. Therefore, we show that spillover rate is not a useful metric for evaluating host jump risk.

2 Introduction

Zoonotic pathogens—defined as animal pathogens that can spill over into humans—are a growing concern to global public health, and it is expected that they will be responsible for the next pandemic (1; 2). Many recognized human pathogens are believed to be of zoonotic origin (3; 4; 5), and a large body of research has focused on identifying characteristics that predispose a pathogen to successfully establishing itself and persisting in a new host species, hereafter referred to as a host jump (6; 7; 8; 9; 10; 11; 12; 13; 14; 5; 15). Spillover—defined as the transmission of a pathogen from a native host species into a novel host species—is a prerequisite to a host jump, and so efforts to reduce host jump risk through spillover prevention have largely focused on pathogens that frequently spill over (16; 17; 18; 19; 20). However, it is unclear how a pathogen's inherent rate of spillover relates to the likelihood of a successful host jump. Put another way, are pathogens that frequently spill over more or less likely to host jump than those that rarely spill over?

At present, the answer to the aforementioned question is unknown and presumably depends on many system-specific details, such as characteristics of the reservoir and novel hosts, the set of all zoonotic pathogens, and other ecological and evolutionary hurdles. However, by considering two pathogens that differ only in their inherent rate of spillover, we can begin to evaluate how spillover rate impacts host jump risk. On one hand, a pathogen that frequently spills over has many opportunities to complete a host jump, so all else equal, a pathogen that spills over more frequently may be conceivably more likely to complete a host jump. On the other hand, a pathogen that has not yet jumped hosts despite spilling over frequently has demonstrated an inability to overcome the ecological and evolutionary hurdles necessary to successfully host jump (21; 18). Whether a pathogen with a high spillover rate is more likely to host jump than a pathogen with a low spillover rate depends on how these two competing factors combine together.

To further illustrate this interplay between spillover rate and host jump likelihood, consider several examples. Rabies lyssavirus, the causative agent of rabies, is estimated to cause tens of

thousands of human rabies cases per year due to zoonotic spillover from dogs and other animal reservoirs (22; 23). Rabies presents a significant public health burden, so preventive measures in place to mitigate spillover are undoubtedly important (24). However, even without these preventative measures and despite the high rate of spillover, few would argue that rabies is a pandemic threat, given the limited opportunities for human-to-human transmission, which would presumably require a human biting another human (25). A similar argument could be made for *Borellia burgdorferi*, the causative agent of Lyme disease, where transmission is limited by the frequency and and duration of ticks feeding on humans (26). In contrast, human immunodeficiency virus (HIV) has completed host jumps into humans on at least two separate occasions (27), and these host jumps occurred after a presumably smaller number of spillover events than the aforementioned pathogens. Despite being a hand-picked list, these examples do illustrate the potential for a disconnect between spillover rate and host jump risk.

Here, we develop a model that provides a quantitative framework for evaluating host jump risk. We derive an analytical solution to this model that depends on the number of past and future spillover events, and on our uncertainty regarding the probability that a single spillover event will result in a host jump. Using this analytical solution, we show that a pathogen's inherent rate of spillover is not predictive of its host jump risk.

3 Model Overview

A successful host jump can be thought of as a two-part process: A pathogen must first spill over into a novel host to cause infection, and then the pathogen must establish sustained transmission in the novel host population. Pathogens must overcome barriers in both of these processes to complete a host jump (20), and can therefore be roughly divided into four categories: "unrestricted", "transmission limited", "spillover limited", and "spillover and transmission limited" (Figure 1A-D). We define "unrestricted pathogens" as those that frequently spill over and are also likely to sustain transmission in the novel host population. "Transmission limited" pathogens

are those that frequently spill over but are unlikely to sustain transmission in the novel host. "Spillover limited" pathogens are those that rarely spill over but are likely to sustain transmission in the novel host if they do. "Spillover and transmission limited" pathogens are those that rarely spill over and are also unlikely to sustain transmission in the novel host population.

The proportion of pathogens that fall within in each of these categories is likely to change over long periods of time, as will our belief in the fraction of pathogens within each group. We show this changing composition in the pool of zoonotic pathogens as a function of how spillover and transmission limited they are in figure 1F, and changes may occur for several different reasons. First, once a pathogen jumps hosts, it changes from being a zoonotic pathogen to being a human pathogen of zoonotic origin, and is therefore removed from the pool of zoonotic threats. Second, when a zoonotic pathogen's successful host jump necessitated substantial evolutionary change the original pathogen might still be considered a zoonotic threat, but the particular evolutionary path followed to result in a host jump was 'used up', making future host jumps less likely. Third, even if the pool of zoonotic pathogens were not changing over time, our belief about the threat it poses would change as more time passes without a host jump. That is, the longer something is a zoonotic threat, the more likely it is to be spillover limited, transmission limited, or both.

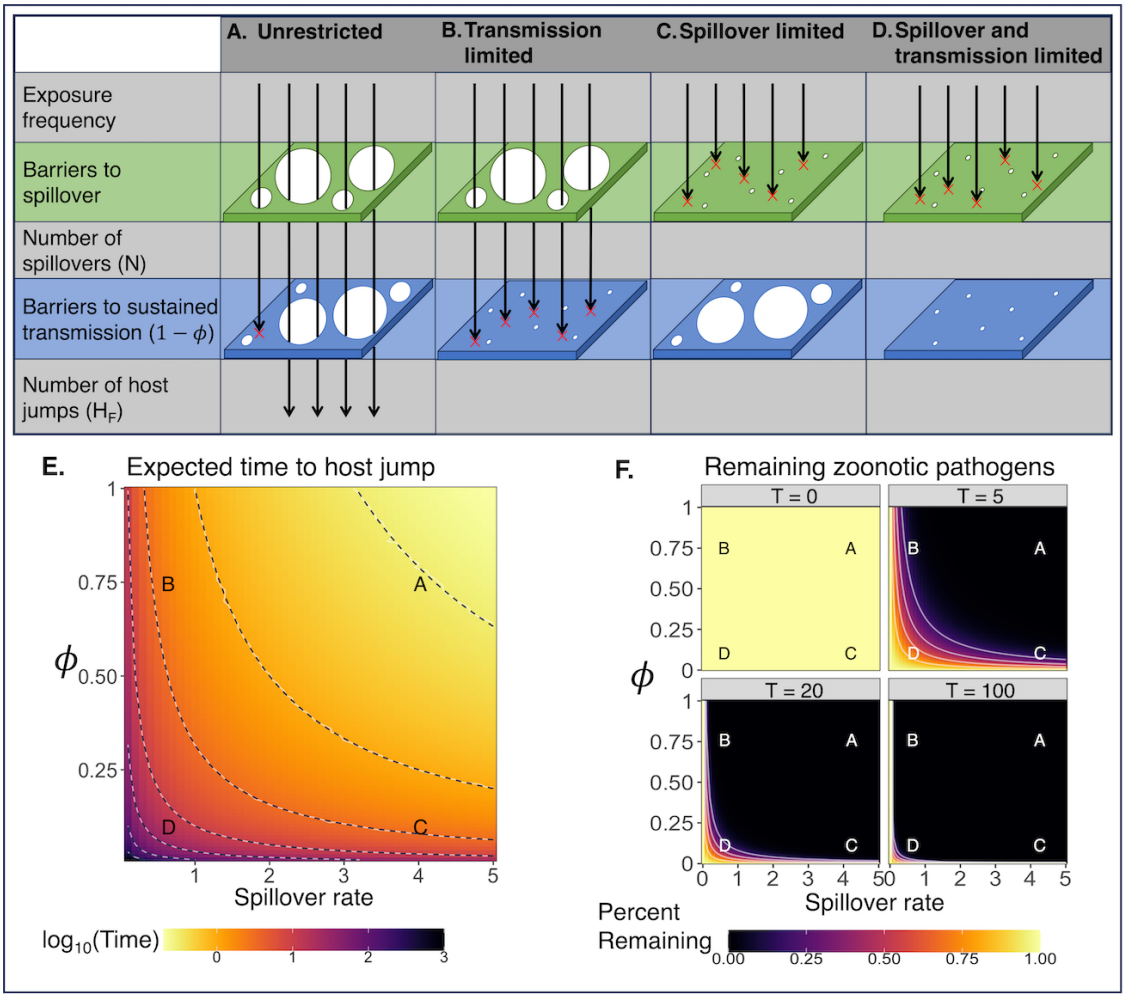

Figure 1: Conceptual characterization of possible pathogen types (**A-D**). In order to successfully host jump, a pathogen must overcome barriers to spillover to successfully infect a novel host ([20]). Following a spillover event, the pathogen must also be able to overcome the ecological and evolutionary barriers to sustained transmission in the novel host ([21]). Pathogens may (or may not) be limited at either step in this process. The expected time until the first successful host jump for these possible pathogen types is shown in **E**. Intuitively, the time to the first host jump decreases as host jump probability (ϕ) and spillover rate (spillovers/T) increase. Unrestricted pathogens have then likely already completed host jumps and have transitioned from being zoonotic pathogens to being human pathogens of zoonotic origin. Thus, the composition of the pool of zoonotic pathogens may change over time, as shown in panel **F**. For illustrative purposes, we assume that at the initial time point (T=0), all pathogens are equally frequent. This panel demonstrates that as time passes, the proportion of "unrestricted" zoonotic pathogens (**A**) decreases quickly for the reasons discussed in the main text, meaning that most of the pool of zoonotic pathogens will be comprised of pathogens that are highly spillover limited (**B**), transmission limited (**C**), or both (**D**).

To develop a quantitative framework for host jump risk, we first quantify the probability that

no host jump will occur in some number of future spillover events (M). We define ϕ as the fixed probability that any given spillover event results in a successful host jump, and we assume the outcome of individual spillovers are independent. Since the outcome of a spillover event is either a host jump or not, we quantify the probability that no future host jumps occur ($H_F = 0$) with a binomial distribution such that

$$P(H_F = 0|\phi,\ M) = (1-\phi)^M \tag{1}$$

In practice, each spillover event would have a unique host jump probability (ϕ_j) that depends on interactions between features of the host, pathogen, and environment. However, Eq. 1 is unchanged even in the presence of this variation, provided ϕ is set to the average of ϕ_j, and the average of ϕ_j does not change over time (Supplemental text 6.1).

Thus, when spillover events are independent, Eq. 1 exactly describes the probability that a zoonotic pathogen will jump hosts and become a human pathogen. One of the key challenges with using this equation, however is that ϕ is generally going to be unknown. Here, we propose that the number of past spillovers (N) can help inform the value of ϕ. To illustrate our logic, consider a pathogen that has spilled over millions of times in the past, but has not yet completed a host jump. Intuitively, its value of ϕ must be very small, since it likely would have jumped hosts otherwise (Figure 1F).

This logic can be formalized by employing tools from Bayesian statistics, in which past observations of spillover that failed to result in a host jump update our belief in the value of a pathogen's ability to successfully host jump following a spillover event (i.e. ϕ). To do so, we treat ϕ as a distribution rather than a fixed constant, where $[\phi]$ is the distribution that describes for our initial uncertainty regarding the value of ϕ (in Bayesian statistics, this is referred to as a prior). One advantage of this approach is that it explicitly allows our uncertainty to be updated in a statistically rigorous way as new data become available. Following standard Bayesian methods, our posterior uncertainty in the value of ϕ can be expressed as:

$$[\phi|N, H_P] = \frac{[\phi] \cdot P(H_P = 0|N, \phi)}{\int_0^1 [\phi] \cdot P(H_P = 0|N, \phi) d\phi} \tag{2}$$

where $P(H_P = 0|N, \phi)$ comes from Eq. 1, using the number of past spillovers (N) in place of M and the number of past host jumps (H_P) in place of H_F. We can use this updated inference on the distribution of ϕ to quantify the probability of at least one host jump in M future spillover events. The product of Eqs. 1, 2 integrated over ϕ gives the probability of no host jumps in M spillovers. Therefore, one minus this quantity gives the probability that, for a given set of pathogens, at least one future spillover event will result in a successful host jump, as shown in equation 3.

$$P(H_F > 0|[\phi], N, M, H_P) = 1 - \int_0^1 [\phi|N, H_P] \cdot P(H_F = 0|M, \phi) d\phi \tag{3}$$

This value is conditional on the number of past spillover events (N), the number of those that resulted in a host jump (H_P), the number of future spillover events (M), and our prior belief about the likelihood that a given spillover event will result in a host jump $[\phi]$. In our analyses, we only consider cases where no past spillover event resulted in a host jump (i.e., $H_P = 0$), but this equation is also valid—although perhaps less useful—for cases where past spillovers have resulted in successful host jumps (Supplemental text 6.2). Note that although the equations presented here assume a fixed number of past and future spillover events (i.e., $P(N = N) = P(M = M) = 1$), this assumption can be readily relaxed (Supplemental text 6.4).

To finish parameterizing our model, it is necessary to define $[\phi]$, which reflects our initial uncertainty regarding the probability that a single spillover event will result in a host jump. However, specifying an appropriate shape for this distribution is not straightforward and may differ for different groups of pathogens. We therefore consider three shapes for this distribution:

1. The vast majority of zoonotic pathogens are unlikely to persist in the novel host, meaning the distribution of ϕ is extremely right-skewed (Fig. 2A).

2. Zoonotic pathogens fall into two distinct sub-classes, where some pathogens are highly

likely to persist in the novel host, and the rest are unlikely to persist, meaning that the distribution of ϕ is "U-shaped" (Fig. 2B).

3. Most zoonotic pathogens are unlikely to persist in the novel host, but a subset have an intermediate chance of persisting, meaning the distribution of ϕ is multi-modal with one peak at 0 and another peak at an intermediate value (Fig. 2C).

Scenario 1 and 2 above can be modeled using a beta distribution and Scenario 3 can be modeled using a mixture of two beta distributions. The results of our analyses are general, but for illustration purposes, we will specify parameter values for each of our prior distributions such that in Scenario 1: $[\phi] \sim \text{Beta}(a = 0.1,\ b = 10)$, in Scenario 2: $[\phi] \sim \text{Beta}(a = 0.1,\ b = 0.1)$, and in Scenario 3: $[\phi] \sim \omega_1 \text{Beta}(a = 0.1,\ b = 10) + \omega_2 \text{Beta}(a = 100,\ b = 500)$; $\omega_1 = 0.8$, $\omega_2 = 0.2$. In Supplemental text 6.2, we show that when $[\phi]$ follows a beta distribution, there is an analytical solution to Eq. 3 such that:

$$P(H_F > 0 | [\phi], N, M, H_P = 0) = 1 - \frac{\Gamma(b+N+M) \cdot \Gamma(a+b+N)}{\Gamma(a+b+N+M) \cdot \Gamma(b+N)} \tag{4}$$

where Γ is the gamma function, and a similar analytical solution exists for beta-mixture distributions (Supplemental text 6.2.1). In what follows, we use Eq. 4 and its beta-mixture analog to explore the role of spillover rate on host jump risk. All main results were also confirmed using simulation (Supplemental text 6.5).

4 Results

We used equation 4 to evaluate the probability of a successful host jump as a function of the number of past and future spillover events, and these analytical solutions are shown for scenarios 1-3 in Fig. 2 panels D-F respectively. In all three scenarios, when only varying the number of future spillover events, the probability of a future host jump increases as the number of future spillovers increases (i.e. host jump probability increases when moving from bottom to top in

Fig. 2D-F). Intuitively, this should be true, as more spillover creates more opportunities for a host jump to occur. In contrast, when only varying the number of past spillover events, increasing the number of spillovers reduces the probability of a future host jump (i.e. host jump probability decreases when moving from left to right in Fig. 2D-F). This can be explained by the increased observation of failed host jumps driving the posterior $[\phi|N, H_P = 0]$ closer to zero, making future host jumps less likely.

The past and future, however, are often correlated. Pathogens that have spilled over frequently in the past will likely continue to spill over frequently in the future, and pathogens that have spilled over rarely in the past will likely continue to spill over rarely in the future. We assess the relationship between spillover rate and the risk of a future host jump under the assumption that the number of past and future spillovers are linearly correlated (for non-linear relationships, see Supplemental text 6.6).

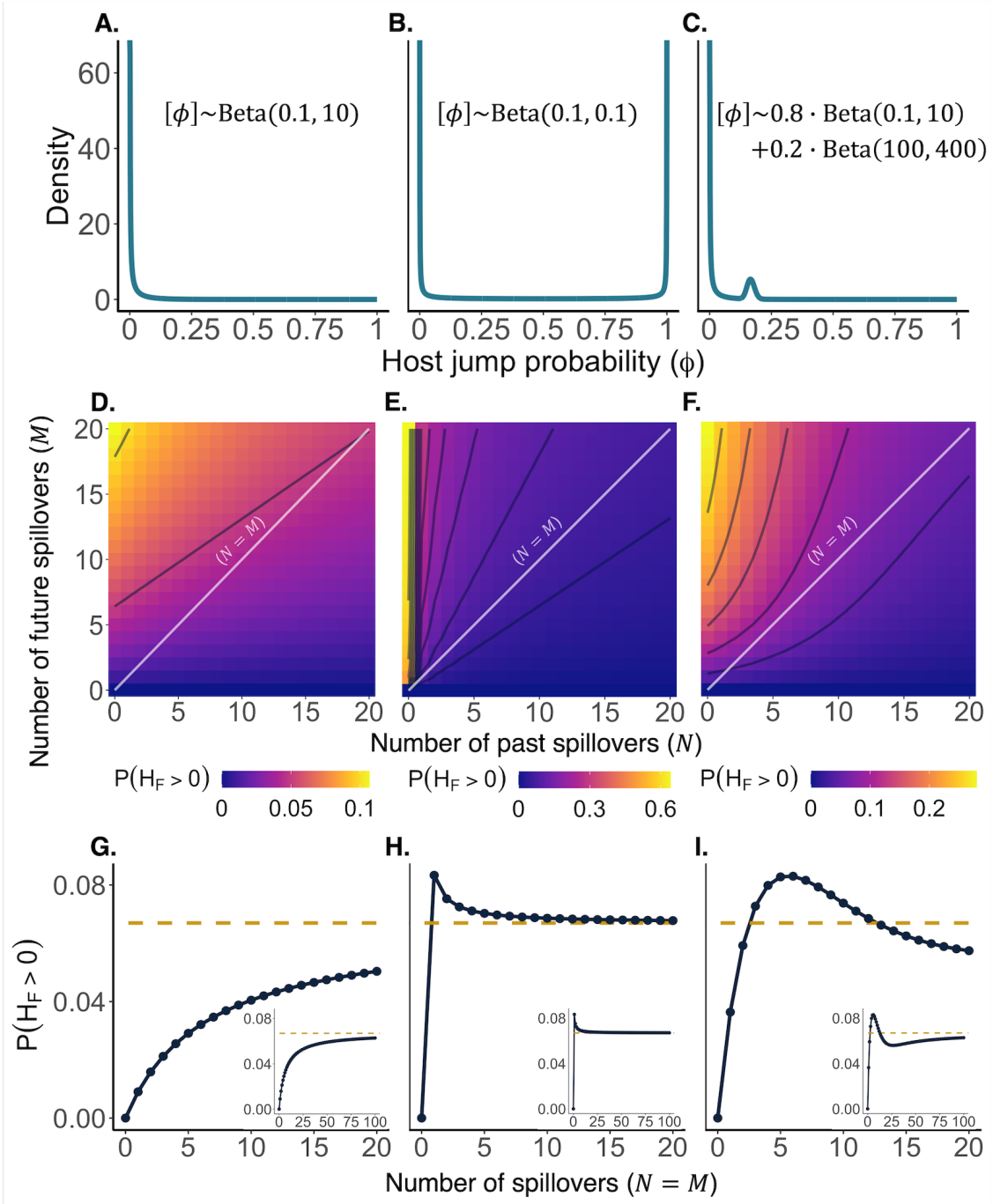

Figure 2: The columns of panels from left to right denote Scenarios 1-3 respectively. Panels A-C show the prior distributions on ϕ. Panels D-F show the model-calculated probability of a successful host jump as a function of the number of past and future spillover events. Host jump risk increases with future spillovers (M) and decreases with past spillover (N). The contour lines in each panel demarcate changes of 5% in total host jump risk. Note that the color range differs for each panel. The solid white lines represent the 1:1 relationship between the number of past and future spillovers, and panels G-I show the probabilities of a future host jump along these lines. Comparing panels G-I reveals that depending on $[\phi]$, host jump risk may increase or decrease as a function of spillover rate. Nevertheless, in all scenarios, host jump risk converges to the value $\left(1 - \frac{1}{(c+1)^a}\right)$, as spillover events increase (inset figures).

For illustrative purposes, we show the case where the number of future spillover events is equal to the number of past spillover events (white 1:1 line in Fig. 2D-F), but note that all of our results are qualitatively similar for other linear correlations (Supplemental text 6.6). Figures 2G-I show how the probability of a host jump varies for zoonotic pathogens that are in all ways equivalent except for differences in their inherent rates of spillover. We find that the level of spillover where host jump risk is greatest depends on the prior $[\phi]$. In Scenario 1 (Fig. 2G), increasing spillover leads to a monotonic increase in host jump probability. In Scenario 2 (Fig. 2H), host jump risk peaks at low rates of spillover and thereafter monotonically decreases. In Scenario 3 (Fig. 2I), host jump risk peaks at an intermediate rate of spillover, declines at slightly higher rates of spillover, and then increases again when rates of spillover become very high. These results therefore illustrate that, when comparing across zoonotic pathogens, even with all else equal, pathogens with high rates of spillover may be more or less likely to cause a host jump than pathogens will low rates of spillover, and the conclusion depends on both our prior uncertainty regarding the value of ϕ and the inherent rate of spillover of the pathogens.

Next, we ask how the probability of a host jump changes as the rate of spillover becomes large. To do so, we evaluate the limit of Eq. 4 as N and M go to infinity. In Supplemental text 6.3, we show that the probability of a host jump converges to $\left(1 - \frac{1}{(c+1)^a}\right)$, where a is the first shape parameter of the beta distribution for prior $[\phi]$ and c is the slope of the linear correlation between the number of spillover events in the past and the future. Notably, this value that the model converges on is intermediate between zero and one for all values of $a, c > 0$. The exact formulation of this limit differs for the beta-mixture distribution, but can still be analytically derived and is functionally similar (Supplemental text 6.3.1). Because the beta shape parameter a is the same for the three scenarios used here, all converge to the same value (the dashed gold lines in Fig. 2G-I). However, they can approach this value from below (i.e., higher rates of spillover lead to an increase in host jump risk) or above (i.e., higher rates of spillover lead to a decrease in host jump risk). This implies that our uncertainty regarding the shape of $[\phi]$ can fundamentally change our conclusion as to whether the greatest host jump risk comes from pathogens that spill

over frequently or those that rarely spill over. In addition, Fig. 2G-I demonstrates that, except at very low rates of spillover, host jump risk changes very slowly relative to the change in spillover rate, meaning that large differences in spillover rate between two zoonotic pathogens will have little predictive power regarding the overall probability that a host jump will occur.

Taken together, these results suggest that for two reasons a pathogen's inherent rate of spillover is not predictive of host jump risk. First, at low levels of spillover, the choice of $[\phi]$ determines whether a pathogen with a low spillover rate or high spillover is more likely to host jump. Second, at high levels of spillover the information gained about ϕ is exactly balanced by the high number of future opportunities for a future host jump to occur. As a result, there is little to no difference in risk between pathogens that spill over at moderate rates or infinitely high rates.

5 Discussion

Here we have derived a general framework to characterize the relationship between the spillover of a zoonotic disease and the probability of that pathogen successfully jumping into a novel host. We derive an analytical solution for this model when our prior distribution on ϕ (the probability that a given spillover event will result in a host jump) follows a beta distribution or mixture of beta distributions. This model demonstrates that, conditional on a pathogen having not yet jumped hosts, future spillover events increase the probability of a host jump while past spillover events decrease the probability of a host jump. We then use this model to ask which is the bigger threat, a pathogen that has rarely spilled over in the past and will rarely spill over in the future, or a pathogen that has frequently spilled over in the past and will frequently spill over in the future. We show that the answer to this question depends on our prior distribution on ϕ. Furthermore, when the rate of spillover is moderate or higher, the difference in spillover rate between pathogens is not as important as one might suspect. While pathogens with high rates of spillover will have many future opportunities to host jump, there is also an increasing amount

of evidence that ϕ is small, given that a host jump has not yet occurred. Our model shows that these competing factors exactly balance each other out as the rate of spillover gets large.

Previous studies addressing host jump risk have largely revolved around identifying underlying drivers of host jump risk based on correlative approaches (28; 21; 29; 30; 31). Here we instead utilize tools from Bayesian statistics to infer how host jump risk changes as a function of the number of past and future spillover events. This approach allows us to explicitly connect a pathogen's rate of spillover with its probability that any given spillover event will result in a host jump (i.e., our parameter ϕ). This connection demonstrates that pathogens with higher rates of spillover in the past must have, on average, lower values of ϕ because if that were not the case, they would have already completed a host jump. Consequently, our model suggests that spillover rate is is a poor predictor of host jump risk. We therefore propose that future efforts to characterize host jump risk should focus not just on the number of spillover events expected in the future and whether the characteristics of that pathogen have been associated with host jumps in other systems, but also on the number of spillover events that have occurred in that system in the past.

Our finding that spillover rate alone is not predictive of host jump risk is driven in part by the competing impacts of spillover rate on host jump risk; higher rates of spillover lead to more opportunities for a host jump to occur, but also indicate that any given spillover is unlikely to result in a host jump (i.e. ϕ is small). This is because pathogens with high inherent rates of spillover must have small values of ϕ on average, as they would have already host jumped otherwise (Fig. 1E and F). In Supplemental text 6.3, we derive that when there is a linear correlation between the number of spillover events in the past and in the future, host jump risk converges on a fixed constant strictly between zero and one as spillover rate gets large. Thus pathogens with moderate or high rates of spillover are nearly equally risky (see Supplemental text 6.7 for an analysis of how the prior on ϕ affects the speed of this convergence). In addition, as we show with Scenarios 1-3, our prior uncertainty in the value of ϕ determines whether we approach this fixed constant from above or from below (i.e. respectively, the riskiest pathogens

are those that spill over rarely or those that spill over frequently). Consequently, when we are unable to reliably quantify our uncertainty in ϕ, spillover is not useful in predicting host jump risk, and even when we are able to quantify its uncertainty, it is only moderately useful. These findings, however, do not undermine the value of spillover prevention, as Eq. 1 demonstrates that decreasing future spillover will decrease host jump risk, regardless of how many times a pathogen has spilled over in the past (see also Fig. 2D-F). Thus efforts to reduce spillover benefit pandemic prevention efforts. It is also worth noting that spillover prevention provides public health benefits even in the absence of host jump risk (32; 24).

Our model illustrates that there are scenarios where host jump risk can be maximized at high, low, or intermediate values of spillover (Scenarios 1, 2, and 3 respectively). Moreover, the analytical solution to our model (Eq. 4) demonstrates that host jump risk prediction is highly dependent on the shape parameters a and b that generate our prior on ϕ (i.e. our uncertainty in the probability that a given spillover event will result in a host jump). Therefore, practical application of our model may then be most useful when the prior on ϕ can be tailored to a particular pathogen or group of pathogens. This approach could account for pathogen-specific details that may not be generalizable to all zoonotic pathogens, such as phylogenetic relationships (14; 31) and genomic markers for the ability to infect and spread in novel hosts (33; 34). Similarly, analyses of past instances of successful host jumps, (13; 35; 29), ranking risk factors (36; 30), and the basic reproductive number, R_0 (28; 37) have been used to quantify host jump risk for different sets of pathogens, and these approaches could also be incorporated into our modeling framework.

Our model results depend on three basic assumptions, namely: 1) the outcome of all spillover events are independent of one another, 2) the average probability that a spillover event results in a host jump (ϕ) is constant over time, and 3) the number of spillovers in the past (N) and future (M) are linearly correlated. Each of these assumptions could be violated in certain situations. Our first assumption could be violated if co-occurring spillover events would affect the probability of either spillover resulting in a host jump. This effect would disproportionately impact pathogens

with high rates of spillover, presumably decreasing the likelihood of a host jump relative to our predictions. Our second assumption, that ϕ is constant over time, could be violated for example due to changes in population density, geographic connectivity, behavior, host immunity, or evolutionary pressure (38). If ϕ were to increase over time, the outcomes of past spillover events would give less information about the risk posed by future spillover events, and we therefore suspect that pathogens with high rates of spillover may pose a relatively greater threat than those with low rates of spillover, but this conclusion would likely depend on the precise way that ϕ is changing over time. Our third assumption that past and future spillovers are linearly correlated seems likely to hold for most pathogens in general. If this assumption were violated, the probability of a host jump would no longer converge to a value between zero and one (dashed gold line in Fig.2G-I), and would instead converge to 0 or 1, depending on whether the correlation is sub-linear or greater than linear (Supplemental text 6.6).

Here, we have proposed a model framework that moves towards a more mechanistic approach to host jump risk prediction. Mechanistic models have been used extensively for predicting timing and location of spillover (17; 39; 40; 41), but this approach has not been used to the same extent for host jump risk prediction (30; 31). We only consider our model to be "semi-mechanistic" in the sense that the underlying characteristics of hosts, pathogens, and the environment that drive host jump risk are only implicitly represented in our prior $[\phi]$. However, incorporating underlying mechanisms of host jump risk explicitly in the construction of the prior distribution $[\phi]$ could serve to improve this approach in the future (28; 21; 42; 10; 29). For instance, features such as phylogenetic or genomic data (43; 44; 14; 34), host-pathogen characteristics (45; 46; 7), and evolutionary theory (37; 28; 47; 48) could all be integrated into characterizing $[\phi]$. Implementing such mechanisms could provide distinct advantages by accounting for biological processes and may be better equipped to preemptively identify zoonotic threats. Combining such a model with efforts to develop therapeutics to “prototype pathogens” could enable rapid pharmaceutical responses to spillover events that are likely to result in a host jump, which could play a significant role in future pandemic prevention (49).

Our model suggests that the relationship between spillover rates and host jump risk can be counter-intuitive: the pathogen that spills over most is not necessarily the greatest host jump threat, nor is it the case that exceptionally rare or undiscovered pathogens pose the greatest risk. Host jump risk is only weakly dependent on a given pathogen's spillover rate. Incorporating system specific factors regarding hosts-pathogen-environment interactions and evolutionary processes will therefore be necessary to more definitively characterize host jump risk for specific pathogens of interest. Efforts to mitigate future spillover will continue to be a powerful pandemic prevention tool (32), but our framework shows that spillover rate alone is a poor predictor of host jump risk.

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