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Mark N. Lurie Brown University

Samantha R. Rosenthal Johnson & Wales University - Providence, Samantha.Rosenthal@jwu.edu

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The Concurrency Hypothesis in Sub-Saharan Africa: Convincing Empirical Evidence is Still Lacking. Response to Mah and Halperin, Epstein, and Morris

Mark N. Lurie and Samantha Rosenthal

Department of Community Health, International Health Institute, Warren Alpert Medical School of Brown University, 121 S. Main Street, Room 221, Providence, RI 02912, USA

We would like to thank the authors for their comments on our article that questioned the amount and quality of the evidence to support the hypothesis that concurrent partnerships are a key driver of the HIV epidemics in Africa [8]. All three letters agree with us that we "raise some valid concerns" that the "evidence for this link is still somewhat limited" [10] and that further research is needed [3,11]. We note further that the three letters were from the most vocal concurrency advocates, and do not necessarily represent mainstream opinion about the current state of knowledge on this important topic [7].

Although the purpose of our article was not to provide an extensive and complete literature review but rather to comment on Mah and Halperin's work (which they themselves called "a selective review" [9]), Epstein faults us for displaying "a highly selective reading" of the literature [3]. Repeating the points made by Mah and Halperin in favor of the concurrency hypothesis would have been redundant; we therefore focused on the abundant contradictory evidence that Mah and Halperin failed to mention.

In the end, the burden is on the advocates of concurrency to use empirical data to prove that concurrency is a driving force of the African HIV epidemics; thus far they have been unable to do so. Association and causation are very different levels of evidence, and our colleagues provide no convincing empirical evidence of causation.

Methodological Issues

Like our original article, the letters raise important methodological issues that make studying the links between concurrency and HIV complex. Interestingly, Morris criticized us for "barking up the wrong evidence tree" but is silent when Mah and Halperin cite studies that use the same methodology and which seem to support the concurrency hypothesis [11]. Mah, Halperin and Epstein are also quick to dismiss on methodological grounds the studies that fail to show an association between concurrency and HIV but repeatedly present studies of the same design when these findings appear to support their hypothesis [3,9–11]. This double standard is unscientific: if the design is flawed, then it is equally flawed for the findings with positive results as for those whose results are negative. And that, in the end, remains our main point: despite the strong conviction of a few scientists, the evidence to support concurrency as the driving force in the Africa HIV epidemics is far from convincing.

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More Concurrency in Africa? Association Does Not Equal Causation

Mah and Halperin cite [10] the 2006 global review of sexual behavior by Wellings and colleagues [18] quoting their conclusion that "concurrent relationships in men in some African countries might have been more common and of longer duration than in other regions." "Might have been" however, is a hypothesis, not convincing evidence.

In addition, Mah, Halperin and Epstein repeatedly cite [4,9,10] a WHO survey as their main source of evidence that there is more concurrency in Africa than elsewhere. Yet this survey, conducted between 1989 and 1990 in 11 countries and published in 1995, is now nearly two decades old; in addition, the survey showed mixed results [2]. There were three countries where a large proportion of men reported concurrent relationships and which also are countries that experienced large HIV epidemics. But there were also countries that have not experienced large HIV epidemics but where a large proportion of men reported concurrent partnerships (for example, Cote d'Ivoire) and there are countries in which a small percentage of men reported concurrency but which did experience large HIV epidemics (for example, Kenya).

Even if some large amount of concurrency could theoretically cause HIV epidemics, the mere existence of concurrency does not mean that it is the driving factor in the vast and varied epidemics seen in sub-Saharan Africa. And even if there were strong ecological evidence that there is more concurrency in Africa than elsewhere, this would be evidence of association, not causation.

Mah and Halperin also argue that it is "highly unlikely...that any form of concurrency would be protective." Yet Reniers and Watkins show, in an ecological study of 34 country-level and 19 sub-country level analyses in Africa, that concurrency in the form of polygyny is actually *negatively* correlated with HIV prevalence [15]. In an accompanying editorial, Kretzschmar and colleagues rightly call for a more careful differentiation between different types of concurrency [7], some forms of which, as we said, may be protective [8].

In addition, a recent population-based study in South Africa that was able to examine causation as a result of their longitudinal design and robust HIV incidence data (nearly 9000 repeat HIV testers and 676 sero-converters) found "no evidence that living in a community with high levels of partnership concurrency increased the risk of acquiring HIV" and concluded that "empirical evidence is needed … before reduction in the levels of concurrent sexual partnerships can be touted as an effective HIV prevention strategy in this setting" [16].

The Qualitative "Evidence"

In terms of the qualitative evidence, Mah and Halperin accuse us of "slight[ing] an entire body of valuable research." We did no such thing. We value qualitative data; it is the *misuse* of qualitative data to which we object. Example: Mah and Halperin [10] cite the Soul City study as part of their "now rather overwhelming evidence" that concurrent relationships are "normalized behavior" in many parts of southern and East Africa, asking "how likely is it that ...only the `right' people were identified in this study?" Answer: very likely. Mah and Halperin fail to point out that the 116 key informant interviews conducted as part of this study selected informants precisely because they were in concurrent relationships, thus demonstrating our point that interviews with a non-random sample of people in any country can reveal that some people are involved in concurrent partnerships. What emerging qualitative studies do show is that there are many different types of concurrent relationships and that treating them all as if they are the same may be counterproductive. And, like ecological studies, qualitative studies offer no evidence of causation.

Mathematical Models

Morris chose not to respond to our criticisms about her model and the parameters used [8, 11]. However, Epstein [3] argues that each parameter used would actually underestimate the effect of concurrency—a dubious and untested hypothesis. For example, she argues that the underestimation of partnership duration in the model would result in an underestimation of the effect of concurrency by "trapping infection for longer times in monogamous pairings." Although this may be true, it is also plausible that increasing relationship duration to more realistic values may actually reduce the total number of partners engaged in concurrency, thus decreasing the effect of concurrency on the spread of HIV. Regardless, both of these assumptions are hypothetical and have not been tested.

Epstein also suggests that introducing transmission probability rates by stage of infection into the model, as we suggested, would increase the effect of concurrency due to the increased transmission probability during acute infection. Yet, studies have debated the contribution that the acute stage of infection has on an HIV epidemic [1,5,13,14]. Abu-Raddad et al., for example, used empirical data from Rakai, Masaka, and the Four-City study to estimate the proportion of infections due to each of the HIV stages and concluded that no HIV stage was dominant in driving the HIV epidemic in sub-Saharan Africa, and that the latent stage of disease provided the greatest contribution.

Finally, Epstein argues that more realistic parameters for the rate of sex acts per partnership would only slow down the epidemic and would not "substantially affect the comparison between serial monogamy and concurrency" because "the fraction of people in the Morris and Kretzschmar model with more than one partner at a time was very low." This is incorrect. The model ran 10 scenarios in which the fraction of partnerships that are concurrent varied from zero to 66% [12]. As a result, we believe that the unrealistic number of sex acts per partnership as well as the extremely high transmission probabilities would have influenced the outcome in profound ways.

Concurrency Interventions: Is There Really "Nothing to Lose"?

Given that the empirical evidence for concurrency is at best mixed, should interventions focus on reducing concurrent relationships? Epstein presents as "fact" that UNAIDS purposely ignored the evidence on concurrency [3] but UNAIDS disagreed, issuing a press release saying that Epstein "makes numerous inaccurate statements which require correction" [17]. Whether UNAIDS deliberately covered up evidence or concluded that on the whole evidence is not yet convincing—as we have argued - remains a contentious issue about which Epstein's "facts" are only one side of the story.

Regardless of what happened in the past, should international agencies focus their resources on attempting to reduce concurrent partnerships? Morris argues that "there is nothing to lose and everything to gain" by intervening to reduce concurrency. We think the issue is more complex than that and that there may be much to lose. Since some concurrent relationships appear to be protective [15], reducing concurrency may not always be a good thing [7,16]. In addition, there is no evidence that messages aimed at reducing concurrency will be successful. Nor is there evidence that a message aimed at reducing concurrency will be any more effective than broader interventions aimed at reducing the total number of partnerships. And how do we know that focused messages to reduce concurrency—like those currently playing on South African radios—won't have an opposite effect than is intended? By focusing messages narrowly on "reducing concurrency" interventions may inadvertently send a message that it is safe to have multiple partners or engage in other risky sexual behaviors, as long as they are not concurrent. The possible unintended consequences, unknown and as yet unmeasured, demonstrate that, if not carefully implemented and closely monitored, there may actually be

much to lose: resources may be misdirected or taken from prevention methods that have proven efficacy, and concurrency interventions may cause confusion and unintended adverse effects.

Conclusion

We believe that an unbiased reading of the evidence about whether concurrency is a driving force in the African AIDS epidemic is decidedly mixed. It may well be that certain forms of concurrency are critically important in certain settings. But we don't yet have sufficient evidence to make such a statement. As the Victorian physicist Lord Kelvin said in 1883, "when you can measure what you are speaking about and express it in numbers you know something about it. But when you cannot measure it, ... your knowledge is of a meager and unsatisfactory kind; it may be the beginning of knowledge, but you have scarcely...advanced to the stage of *Science*, whatever the matter may be" (Kelvin quoted in Weiner [6]).

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