Social Science & Medicine 139 (2015) 26–35

Contents lists available at ScienceDirect

Social Science & Medicine

journal homepage: www.elsevier.com/locate/socscimed

Review article

Syndemics of psychosocial problems and HIV risk: A systematic review of empirical tests of the disease interaction concept

Alexander C. Tsai [a, b, c, *], Bridget F.O. Burns [a]

[a] Center for Global Health, Massachusetts General Hospital, Boston, MA, United States
[b] Harvard Center for Population and Development Studies, Cambridge, MA, United States
[c] Mbarara University of Science and Technology, Mbarara, Uganda

ARTICLE INFO

Article history:
Received 27 February 2015
Received in revised form
11 June 2015
Accepted 22 June 2015
Available online 29 June 2015

Keywords:
AIDS/HIV
Social determinants

ABSTRACT

In the theory of syndemics, diseases co-occur in particular temporal or geographical contexts due to harmful social conditions (*disease concentration*) and interact at the level of populations and individuals, with mutually enhancing deleterious consequences for health (*disease interaction*). This theory has widespread adherents in the field, but the extent to which there is empirical support for the concept of disease interaction remains unclear. In January 2015 we systematically searched 7 bibliographic databases and tracked citations to highly cited publications associated with the theory of syndemics. Of the 783 records, we ultimately included 34 published journal articles, 5 dissertations, and 1 conference abstract. Most studies were based on a cross-sectional design (32 [80%]), were conducted in the U.S. (32 [80%]), and focused on men who have sex with men (21 [53%]). The most frequently studied psychosocial problems were related to mental health (33 [83%]), substance abuse (36 [90%]), and violence (27 [68%]); while the most frequently studied outcome variables were HIV transmission risk behaviors (29 [73%]) or HIV infection (9 [23%]). To test the disease interaction concept, 11 (28%) studies used some variation of a product term, with less than half of these (5/11 [45%]) providing sufficient information to interpret interaction both on an additive and on a multiplicative scale. The most frequently used specification (31 [78%]) to test the disease interaction concept was the sum score corresponding to the total count of psychosocial problems. Although the count variable approach does not test hypotheses about interactions between psychosocial problems, these studies were much more likely than others (14/31 [45%] vs. 0/9 [0%]; $\chi 2 = 6.25$, $P = 0.01$) to incorporate language about "synergy" or "interaction" that was inconsistent with the statistical models used. Therefore, more evidence is needed to assess the extent to which diseases interact, either at the level of populations or individuals, to amplify HIV risk.

1. Introduction

The poor and underserved often face a complex constellation of health and social problems that conspire to undermine their wellbeing. The term "syndemic" was proposed by Singer (1994) to call attention to these issues, with a special focus on the frequently co-occurring problems of substance abuse, violence, and HIV (Singer, 1996, 2006). As originally described and summarized in several publications (Singer, 1994, 1996, 2006), two characteristics are central to his conceptualization of a syndemic. First, diseases co-occur in particular temporal or geographical contexts due to harmful social conditions (*disease concentration*). Second, diseases interact at the level of populations and individuals, with mutually enhancing deleterious consequences for health (*disease interaction*). As summarized by Singer and Clair (2003) in one of the more recent restatements of the theory, "a syndemic is a set of intertwined and mutually enhancing epidemics involving disease interactions at the biological level that develop and are sustained in a community/population because of harmful social conditions and injurious social connections" (p.429). In one of the first empirical studies in this literature, Stall et al. (2003) attempted to extend conceptual thinking about syndemics to understanding HIV risk among men who have sex with men in the U.S. While their analysis did not provide evidence of interacting epidemics, they did show that psychosocial problems were frequently co-occurring and that men with a greater number of psychosocial problems were more

* Corresponding author. MGH Global Health, Suite 722, 125 Nashua Street, Boston, MA 02114, United States.
E-mail address: actsai@partners.org (A.C. Tsai).

http://dx.doi.org/10.1016/j.socscimed.2015.06.024
0277-9536/

vulnerable to HIV.

The theory of syndemics is consistent with previously published theories that have been deployed to explain the existence of health disparities, including the social origins of greater health risks among the marginalized and dispossessed (Farmer, 1999, 2004; Link and Phelan, 1995; Scheper-Hughes and Bourgois, 2004) and the role of historically ingrained forces in exerting conjoint influences on HIV risk (Farmer, 1996; Farmer et al., 1993). The harmful effects of co-occurring psychosocial problems have also been highlighted in other literature that have evolved largely in parallel to the literature on syndemics, including the concepts of multimorbidity (van den Akker et al., 1996; van den Akker et al., 1998) and dual diagnosis (Drake et al., 1991; Lehman et al., 1989). In this regard, the concept of disease concentration is empirically well established. However, the extent to which there is empirical support for disease interaction in HIV risk remains unclear. While the theory of syndemics would remain useful for its conceptualization of disease concentration even if the concept of disease interaction were to fail empirical testing, this is an important gap in the literature because of the overall programmatic and policy importance of the syndemics orientation. A decade ago, Gerberding (2005) described U.S. Centers for Disease Control and Prevention (CDC) efforts to transform health protection research with the aim of reducing health disparities. Although complex systems theories and a syndemics orientation were explicitly incorporated into her vision for the CDC's future, she also noted that “application of complex systems theories or syndemic science to health protection challenges is in its infancy” (p.1405). While public health researchers motivated by an interest in improving health and wellbeing in vulnerable populations have made important progress in utilizing and understanding the theory of syndemics, to date there has been no systematic summary of how the concept of disease interaction in syndemic theory has been tested in empirical work.

2. Conceptual framework

The concept of disease interaction has had a long and controversial history in the epidemiologic literature (Blot and Day, 1979; Greenland, 2009; Kaufman, 2009; Kupper and Hogan, 1978; Rothman, 1974, 1976a; Rothman et al., 1980; Saracci, 1980; Siemiatycki and Thomas, 1981; VanderWeele, 2009a; Walter and Holford, 1978). Summarized succinctly, there are two different concepts of interaction that should be distinguished: the theoretical concept of causal interaction (formerly described as “biologic interaction”), and statistical interaction. The notion of *causal interaction* is derived from a theoretical concept of causation and was originally proposed by Rothman (1974), who formally defined it as a deviation from additivity of the risk differences of the causal risk factors under investigation. A greater than additive deviation is typically described as synergy, or a positive or super-additive interaction; while a less than additive deviation is typically described as antagonism, or a negative or sub-additive interaction (Rothman, 1974, 1976b; VanderWeele and Knol, 2014). *Statistical interaction*, on the other hand, refers to a situation in which an additional parameter is required for a statistical model to adequately describe joint exposure to the risk factors under investigation. In contrast to the concept of causal interaction, which necessarily entails a concern about deviation from additivity, statistical interaction is dependent upon the underlying scale: if an additive model is employed, a statistically significant product term indicates deviation from additivity, whereas a statistically significant product term in a multiplicative model indicates deviation from multiplicativity.

In a linear (e.g., least squares) regression model fitted to a dataset in order to better understand the relationship between a dichotomous outcome variable Y and two dichotomous explanatory variables X_1 and X_2, a simple test for causal interaction between X_1 and X_2 in the absence of confounding might proceed as follows:

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_1 X_2$$

where, for example, Y may represent HIV infection or a risk factor for HIV infection, e.g., condomless sexual intercourse with a nonprimary partner; while X_1 and X_2 may represent psychosocial problems such as substance abuse and intimate partner violence. In this model, it is apparent that the main effects of X_1 and X_2, assuming that there is no effect of the other covariate, are given respectively as:

$$Y_{X_1=1,X_2=0} - Y_{X_1=0,X_2=0} = \beta_0 + \beta_1 - \beta_0 = \beta_1$$

$$Y_{X_1=0,X_2=1} - Y_{X_1=0,X_2=0} = \beta_0 + \beta_2 - \beta_0 = \beta_2$$

and that the combined effect of X_1 and X_2, compared with no effect of X_1 and X_2, is given by adding the estimated regression coefficients on X_1, X_2, and their product X_1X_2:

$$Y_{X_1=1,X_2=1} - Y_{X_1=0,X_2=0} = \beta_0 + \beta_1 + \beta_2 + \beta_3 - \beta_0 = \beta_1 + \beta_2 + \beta_3$$

If $\beta_3 > 0$, then the combined effect of X_1 and X_2 is greater than their sum $(\beta_1 + \beta_2)$ and there is said to be a greater than additive deviation, or a positive or super-additive interaction. If $\beta_3 < 0$, then the combined effect of X_1 and X_2 is less than their sum $(\beta_1 + \beta_2)$ and there is said to be a less than additive deviation, or a negative or sub-additive interaction. If $\beta_3 = 0$, then the combined effect of X_1 and X_2 is equal to the sum $(\beta_1 + \beta_2)$ and there is said to be no deviation from additivity, or no interaction; by dint of their inclusion in a regression model that is linear in its parameters, X_1 and X_2 are said to have “additive” effects on the outcome.

Although use of least squares to model a *dichotomous* outcome variable is generally shunned by physicians and epidemiologists, it is standard practice among economists and is frequently referred to as the linear probability model (Angrist and Pischke, 2009; Wooldridge, 2010). Two minor disadvantages of the linear probability model are that it generates heteroskedastic standard errors and predicted values of Y that may lie outside of the interval [0,1] (Goldberger, 1964). However, as Wooldridge (2010) notes, “If the main purpose is to estimate the partial effect of [the independent variable] on the response probability, averaged across the distribution of [the independent variable], then the fact that some predicted values are outside the unit interval may not be very important” (p.455). In addition, any potential bias is lessened as the relative proportion of predicted probabilities lying inside the unit interval increases (Horrace and Oaxaca, 2006). And finally, the standard errors can easily be corrected using heteroskedasticity-consistent robust estimates of variance (Huber, 1967; White, 1980). Furthermore, a considerable advantage of the linear probability model that is germane to testing the theory of syndemics is that it is an additive model; therefore, given the usual assumptions, an estimate for the parameter β_3 is a test for causal interaction and summarizes the extent to which a departure from additivity is observed. The estimated regression coefficients can easily be interpreted as marginal effects with no additional computation required.

Although the linear probability model has many attractive features to recommend it, because of the disadvantages described above, the logit transformation is generally favored by many in the field: