

The Latino Mortality Paradox: A Test of the "Salmon Bias" and Healthy Migrant Hypotheses

ABSTRACT

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Objectives. Relative to non-Latino Whites, Latinos have a worse socioeconomic profile but a lower mortality rate, a finding that presents an epidemiologic paradox. This study tested the salmon bias hypothesis that Latinos engage in return migration to their country of origin and are thereby rendered "statistically immortal" and the alternative hypothesis that selection of healthier migrants to the United States accounts for the paradox.

Methods. National Longitudinal Mortality Study data were used to examine mortality rates of the following groups for whom the salmon hypothesis is not feasible: Cubans, who face barriers against return migration; Puerto Ricans, whose deaths in Puerto Rico are recorded in US national statistics; and US-born individuals, who are not subject to either salmon or healthy migrant effects.

Results. The sample included 301 718 non-Latino Whites and 17 375 Latino Whites 25 years or older. Cubans and Puerto Ricans had lower mortality than non-Latino Whites. Moreover, US-born Latinos had lower mortality than US-born non-Latino Whites.

Conclusions. Neither the salmon nor the healthy migrant hypothesis explains the pattern of findings. Other factors must be operating to produce the lower mortality. (*Am J Public Health.* 1999;89:1543-1548)

Numerous studies have indicated that lower socioeconomic status (SES) is related to poor health, in terms of both morbidity and mortality.¹ Compared with non-Latino Whites, Latinos have higher poverty rates, less education, and less health insurance² but a lower all-cause mortality rate.^{3,4} The National Longitudinal Mortality Study (NLMS)⁵ revealed lower income-adjusted mortality rates for cancer, cardiovascular disease, and all-cause mortality among Latinos relative to non-Latino Whites. Data from the National Health Interview Survey (NHIS) replicated these findings, especially among middle to older age groups.⁶ Latino mortality stands in sharp contrast to that of African Americans, who, like Latinos, have a lower SES profile than Whites but a higher mortality rate.^{6,7} Thus, Latino mortality presents an epidemiologic paradox.³

Much controversy surrounds the paradox.^{3,6,8} Competing explanations fall into 2 broad categories. The first centers on the premise that the lower mortality is "real" and is the result of more favorable health behaviors, risk and genetic factors, and greater family support among Latinos than among non-Latino Whites.^{3,9,10} The second postulates that the lower mortality is not "genuine" but rather is caused by migratory factors.

One hypothesis suggests that the selection of healthy Latino migrants into the United States accounts for the paradox.^{5,11} International data indicate, for example, that the mortality rate is lower in immigrants than in their country of origin.¹² US data show that foreign-born individuals have better health (e.g., self-reported health, less activity limitation and bed days) than US-born respondents, and recent Latino immigrants are healthier than those residing in the United States for longer periods.¹³

A second migratory hypothesis is the "salmon bias,"¹⁴ which proposes that, reflecting the desire to die in one's birthplace, many Latinos return to their country of birth after

temporary employment, retirement, or becoming seriously ill.^{11,14} Because foreign deaths are not tabulated in US mortality statistics, some individuals are rendered "statistically immortal,"^{14(p1237)} resulting in an artificially low Latino mortality rate.

Although the salmon bias hypothesis has not been tested, some evidence suggests that it is plausible. One study¹⁵ estimated return migration rates of various foreign-born groups based on data from a program requiring immigrants to submit yearly address reports to the Immigration and Naturalization Service. Lower- and upper-bound return migration estimates (assuming a 50% and 100% response rate for filing address reports) ranged from 15.6% to 56.2% for Mexicans, 52.4% to 72.5% for South Americans, and 49.6% to 69.5% for Central Americans and Caribbean persons (excluding Cubans). Although return migration (both permanent and temporary) depends on specific community, economic, and social network factors,^{16,17} it can be substantial. As many as 75% of households in Mexican migrant towns engage in return migration from the United States.¹⁸ Despite the methodologic shortcomings and the specificity of communities surveyed, these studies suggest that the salmon effect and healthy migrant hypothe-

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ses present potential biases in US Latino mortality rates.

A systematic investigation of the Latino mortality paradox requires that artifactual hypotheses be tested first. If these can be dismissed, subsequent studies can then pursue substantive hypotheses with confidence that the lower mortality is "real." The purpose of the present investigation, therefore, was to test the salmon bias and healthy migrant hypotheses.

Methods

The Salmon Bias Hypothesis

The need to trace immigration patterns of large samples of Latinos creates formidable barriers for prospective studies of the salmon bias hypothesis. However, the hypothesis can be tested indirectly by capitalizing on the heterogeneity of Latinos in the United States. Latinos differ in SES, political and immigration history, nativity status (foreign vs US birth), and access to country of origin.^{2,19,20} Because the salmon bias is a near impossibility for some groups, mortality rates should be lower only among groups for which the salmon effect is plausible.

Cubans and Puerto Ricans. Cubans and Puerto Ricans are *not* subject to the salmon effect but for different reasons. Cubans cannot return easily to their home country. Although Puerto Ricans have access to their homeland, deaths occurring in Puerto Rico (a US commonwealth) are tabulated in US mortality statistics.⁸ If the salmon bias accounts for the mortality paradox, Cubans and Puerto Ricans should not have lower mortality than Whites. Instead, lower mortality should be observed among other groups, such as Mexicans, Central and South Americans, and other Latinos.

US-Born and Foreign-Born Latinos. Among Latinos, *familism* is a strong cultural value and resource.^{21,22} Although familism would motivate foreign-born Latinos to return home (to be among the relatives they left), it would keep US-born Latinos from leaving the families they established in the United States. This premise holds even among Mexican Americans, who have relatively easy access to Mexico.¹⁸ Community studies of Mexicans in the United States indicate that, compared with their immigrant counterparts, US-born Mexicans have more extensive social networks and interact more with intergenerational family members and friends in the United States.²³ Furthermore, among legal male immigrants, being married and having children (migrant or US-born children) decrease the odds of return migration to Mexico.¹⁸

Given that foreign-born Latinos have a stronger motive to leave the United States

than US-born Latinos, 2 additional tests of the salmon hypothesis are possible. First, US-born Latinos, who are unlikely to leave the United States, should not have lower mortality than US-born Whites. If, however, US-born Latinos still have better health than their US-born White counterparts, it cannot be attributed to the salmon effect. Second, because foreign-born Latinos may be motivated to leave the United States, mortality rates should be lower among foreign-born than US-born Latinos. This finding, however, would not unequivocally confirm the salmon hypothesis, because other explanations are possible—especially selective migration of healthier workers to the United States (see next section). If, in contrast, mortality is higher among foreign-born than US-born Latinos, it would cast doubt on the salmon bias and healthy migrant hypotheses. Higher mortality rates in foreign-born Latinos could be explained by factors such as the stress of immigration or the longer exposure of the native born to better health care in the United States.

The Healthy Migrant Hypothesis

The healthy migrant hypothesis also presents a number of methodologic challenges. Nonetheless, it can be tested by examining the mortality of US-born and foreign-born groups.

US-Born Individuals. Because they are not immigrants, US-born individuals are not subject to migratory selection processes. Therefore, if the Latino mortality paradox remains when only US-born Latinos are compared with US-born non-Latino Whites, some mechanisms other than selective migration must be involved.

Foreign-Born Individuals. If the healthy migrant effect is mainly responsible for the superior health of Latinos, selection factors should operate only among foreign-born Latinos. Because all immigrants are subject to selection, the healthy migrant hypothesis would not predict a health benefit for foreign-born Latinos relative to foreign-born non-Latino Whites (e.g., born in European countries). If, however, foreign-born Latinos had lower mortality than their White counterparts, the healthy migrant hypothesis could not account parsimoniously for this finding. Even if the healthiest migrate from places where death rates differ, and Latino countries have the lowest rates, the selection hypothesis would have to be modified to explain why Latinos are healthier before migration.

Data Source

To test the salmon bias and healthy migrant hypotheses, we used a subset of data

from the study by Sorlie and colleagues.⁵ Given the different aims of our study, our analytic strategies differed from those of Sorlie and colleagues. The most notable differences involved our more detailed comparisons of various Latino groups, as well as of foreign- and US-born respondents, and a somewhat more comprehensive control of SES that includes both education and income.

The data used were from the NLMS Public Use File (Release 2, October 1995), which contains a representative sample of the noninstitutionalized US population. The NLMS links data from 2 sources: (1) the Current Population Survey, conducted by telephone and personal interview by the US Bureau of the Census, with a response rate of nearly 96%, and (2) the National Death Index, a computer file of deaths recorded by the National Center for Health Statistics. Release 2 of the NLMS Public Use File links 5 Current Population Surveys conducted between 1979 and 1981 to the National Death Index for the period 1979–1989, yielding up to 9 years of follow-up mortality data. The public use file is a subset of the larger NLMS used in Sorlie and colleagues' study, which contains 12 Current Population Surveys conducted between 1973 and 1985.⁵

The total sample consisted of 319 093 individuals (53% female) 25 years or older. Of these, 301 718 (94.6%) were non-Latino Whites and 17 375 (5.4%) were Latino (Whites). These percentages are comparable to the US census data during the period under study (in 1980, Latinos constituted 5.1% of the total US population⁸). Table 1 shows the sample sizes of the various ethnic groups and other demographic characteristics.

Latino ethnic group was determined by asking respondents about their national or cultural group of origin. In this study, responses were coded as (1) Mexican (including Mexican American, Chicano, or Mexican/Mexicano), (2) Puerto Rican, (3) Cuban, and (4) Central or South American or "other" Spanish. (Although the latter is a heterogeneous group, the sample size did not allow for further subdivisions.) Respondents were also asked about their race. We selected only White Latinos and non-Latinos for all analyses to eliminate the confounding effect of race. Only 785 Latinos, or 2% of the total number of Latinos in the full NLMS data set, were excluded by this criterion. Although race and SES are correlated in Latino populations, this procedure did not produce a biased, middle-class Latino sample (see Table 1).

All analyses controlled for SES, age, and sex. SES was adjusted on the basis of income (assessed as total family income during the past 12 months adjusted for inflation

to 1980 dollars) and educational attainment (8 categories: elementary grades 0-4, 5-7, 8; high school years 1-3, 4; college years 1-3, 4, 5 or more). Age reflects age at the time of the Current Population Survey. Sex was coded as male or female.

Place of birth was coded as US-born if the respondent stated that he or she was born in 1 of the 50 states or as foreign-born (i.e., rest of the world). Respondents who identified themselves, for example, as Mexican and foreign-born were assumed to have been born in Mexico, but their birthplace was coded as "rest of world" in the NLMS. Not all Current Population Survey interviews, however, surveyed respondents about their place of birth. Data on place of birth were available for 259 057 respondents (81.2% of the total NLMS sample 25 years or older). Of these, 246 639 (95.2%) were non-Latino Whites and 12 418 (4.8%) were Latinos. This subset of the sample with available place-of-birth data was not a biased subsample of the full NLMS. Because the sampling strategy in each Current Population Survey produced a representative sample of the noninstitutionalized US population, missing data on place of birth did not introduce a systematic bias. The proportional distribution of cases with missing data on place of birth, for example, was similar across sex, Latino groups, and non-Latino Whites.

The outcome variable—mortality status—was coded in the NLMS as alive or dead on the basis of National Death Index data. Several studies have found the National Death Index to be a valid source of mortality data by using personal identifiers and the Current Population Survey–National Death Index matching procedure to be reliable.^{5,24} The linkage procedure used 14 personal identifiers, allowing for matches even when some information was missing or incongruent (e.g., social security number, surname).⁸

Data Analysis

Cox proportional hazards models²⁵ adjusted for education and income (treated as covariates in the models) were used to estimate the relative mortality rate. Most results are presented by sex and age.

Results

We first examined ratios of death rates for different Latino subgroups. Table 2 shows results of the Cox proportional hazards models, adjusted for age, education, and income. For each of the 4 Latino groups, men and women had lower death rates than their non-Latino White counterparts. The lower mortality of Puerto Ricans and Cubans is of particu-

TABLE 1—Sample Size of Various Groups, Number of Deaths, and Demographic Characteristics

	n	%	No. of Deaths	Education (Median)	Income, \$ (Median)	Age, y (Mean)
Non-Latino Whites	301 718	94.6	34 999	HS grad	15–20k	48.5
Mexican	10 230	3.2	553	Some HS	10–15k	41.8
Puerto Rican	1 910	0.6	87	Some HS	10–15k	41.6
Cuban	1 123	0.4	75	HS grad	15–20k	49.3
Central/South American	1 380	0.4	39	HS grad	10–15k	40.3
Other Latino	2 732	0.9	210	HS grad	10–15k	46.6
Total N	319 093					

Note. HS grad = high school graduate; k = 1000. Only White respondents (Latinos and non-Latinos) and adults 25 years or older were included in the study. The number of Latinos in the sample was 17 375 (5.4% of total sample).

lar interest, given the implausibility of the salmon hypothesis for these groups. Both groups are likely to be fully represented in US mortality statistics regardless of whether they are foreign- or US-born.

The paradox of lower mortality among Puerto Ricans and Cubans cannot be attributed to the salmon bias. However, to test this hypothesis in the other groups, we next conducted analyses by foreign- vs US-born status, excluding Puerto Ricans and Cubans. (We performed the identical analyses using the full sample, and the results remained essentially unchanged.) As stated earlier in this paper, not all of the Current Population Surveys asked respondents about their birthplace. This reduced sample sizes for these comparisons.

Cox proportional hazards models, adjusted for education and income, were used to compare US- and foreign-born men and women in different age groups. The first 3 columns of Table 3 show the hazard rate ratios of US-born Latinos, foreign-born Latinos, and foreign-born non-Latino Whites compared with US-born non-Latino Whites (reference group); the fourth and fifth columns show the hazard rate ratios of foreign-born Latinos compared with US-born Latinos and foreign-born non-Latino Whites.

Column 1 of Table 3 indicates that US-born male and female Latinos had lower overall mortality than did US-born Whites. Insofar as US-born Latinos are unlikely to move to a foreign country, these results do not support the salmon hypothesis. In addition, because US-born Latinos are not immigrants, these findings do not support the healthy migrant selection hypothesis.

In columns 2, 3, and 4, if either the salmon effect or the healthy migrant effect is operating, mortality should be lower among the foreign- than among the US-born. Column 2 indicates that foreign-born Latinos had a health advantage over US-born Whites. Column 3 shows that foreign-born non-

Latino Whites had lower mortality than US-born Whites among 3 groups, young and middle-aged men and middle-aged women. Older foreign-born women had slightly higher mortality than their US-born counterparts. Some caution should be exercised when examining the results in column 4, because the number of deaths in some age groups was low. (For the analyses in Column 4 of Table 3, the average power [across men and women] to detect a 25% decrease in mortality among the foreign-born was only 35%. This indicates that there was low power to detect a statistically significant decrease in mortality among the foreign- relative to the US-born. Although power was higher for older men and women [61% and 51%, respectively], it was only 16% for young women. Despite low power, we present these data because they provide additional tests of the salmon bias and healthy migrant hypotheses and because they are comparable to the effects found for non-Latino Whites in column 3.) In 2 groups—middle-aged men and women—foreign-born Latinos had lower mortality than US-born Latinos. A third group, young female Latinas, also had a hazard ratio much lower than 1, but it was not significant (but see foregoing parenthetical discussion of analyses in column 4).

Note that a similar effect of better health among the foreign-born also occurred in 3 non-Latino White groups in column 3. The findings concerning the foreign-born raise the possibility of salmon bias and healthy migrant effects that extend to both non-Latinos and Latinos. Recall, however, that in column 1, US-born male and female Latinos also had better health than their US-born non-Latino counterparts. Clearly, the healthy migrant and salmon bias hypotheses do not support the observed mortality pattern.

Column 5 in Table 3 shows that for men and women in all but the youngest age groups,

TABLE 2—Hazard Ratios of Mortality in Latino Groups Compared With Non-Latino Whites^a

	Men Hazard Ratio (95% CI)	Women Hazard Ratio (95% CI)
Mexican	0.57 (0.52, 0.65)	0.60 (0.52, 0.69)
Puerto Rican	0.63 (0.48, 0.82)	0.45 (0.32, 0.64)
Cuban	0.53 (0.39, 0.72)	0.47 (0.33, 0.66)
Central or South American and other Latino	0.61 (0.52, 0.72)	0.56 (0.46, 0.69)
All Latinos/Latinas	0.59 (0.54, 0.64)	0.56 (0.51, 0.62)

Note. CI = confidence interval. Age was a categorical variable, with 65 years or older as the reference group (coded 0), and ages 0 to 24 were excluded. None of the confidence intervals contain 1.00.

^aEstimated by Cox proportional hazards model, with adjustment for age, household income, and education.

foreign-born Latinos had lower mortality than their foreign-born non-Latino White counterparts. As with the previous set of results, it is difficult to explain these findings parsimoniously with either the healthy migrant or the salmon bias hypothesis. The healthy migrant hypothesis would have to be qualified to allow Latino migrants to be healthier than non-Latino White migrants. The salmon bias hypothesis would be tenable for the results only if a proximity¹⁵ clause were added, stating that foreign-born Latinos engage in return migration because their homelands are closer to the United States than those of non-Latino White immigrants. Thus, the pattern of results in Table 3 suggests that the salmon effect and healthy migrant hypotheses do not adequately account for the Latino mortality paradox.

Discussion

The salmon bias hypothesis does not explain the lower mortality among Latinos.

Most persuasive are the comparisons involving Cubans and Puerto Ricans. For these groups, the salmon bias is not likely to occur, but for different reasons. Cuba is not easily accessible, and the political conditions that prompted Cubans to migrate still exist, making return migration unappealing. Puerto Ricans can return to their country of origin, but deaths occurring in Puerto Rico are tabulated in the National Death Index. Nonetheless, Puerto Ricans and Cubans had lower mortality than Whites.

The lower mortality among the Cubans, the overwhelming majority of whom are foreign-born, may be due to selection of healthier immigrants.²⁶ This theory is particularly plausible because the data used in this study were from 5 Current Population Surveys that were conducted between 1979 and 1981. By that time, waves of the predominantly working- to upper-class Cuban refugees had arrived in the United States.^{19,20} In terms of SES, the most disadvantaged Cubans arrived in 1980 and subsequent years. It is likely,

therefore, that the Current Population Survey used in this study included very few of these more recent and probably less healthy immigrants.

The salmon bias hypothesis cannot account for the lower mortality among Puerto Ricans or Cubans. In addition, in the remaining Latino groups, comparisons involving nativity status provided evidence inconsistent with a salmon hypothesis. For both men and women, mortality was lower even among US-born Latinos relative to US-born non-Latino Whites (Table 3, column 1). Based on the premise that US-born individuals have less motivation to leave the United States, this finding is evidence against a salmon bias.

The healthy migrant hypothesis does not account for the mortality paradox either. In most comparisons of foreign-born male and female Latinos with their foreign-born White counterparts, Latinos still had lower mortality. It is important, as noted earlier, that US-born Latinos (who are not subject to migration selection factors) had a health advantage over US-born non-Latino Whites. The pattern of findings therefore suggests that other factors must be involved in producing the lower Latino mortality.

If the salmon bias and healthy migrant hypotheses are implausible, what accounts for the paradox? One possibility is that differences in health behaviors (e.g., diet, smoking) favor Latinos.^{3,9,10} Relative to non-Latino Whites, Latinos have a health advantage for cardiovascular disease, cancer from all causes, and cancer of the lung, colon, breast, and prostate.^{3-5,27,28} Male and female Latinos are less likely to drink alcohol,^{29,30} and Latina women are less likely to smoke than non-Latino Whites.^{29,31} Both alcohol and cigarette smoking are major risk factors for cancer and heart disease.

TABLE 3—Hazard Ratios of Mortality in Latinos, Excluding Cubans and Puerto Ricans, and Non-Latino Whites Compared With Various US-Born and Foreign-Born Groups^a

Age, y	US-Born Latinos vs US-Born Whites, Hazard Ratio (95% CI)	Foreign-Born Latinos vs US-Born Whites, Hazard Ratio (95% CI)	Foreign-Born Non-Latino Whites vs US-Born Whites, Hazard Ratio (95% CI)	Foreign-Born Latinos vs US-Born Latinos, Hazard Ratio (95% CI)	Foreign-Born Latinos vs Foreign-Born Whites, Hazard Ratio (95% CI)
Men					
25-44	0.59 (0.44, 0.80) ^b	0.56 (0.37, 0.85) ^b	0.51 (0.32, 0.81) ^b	1.12 (0.62, 2.03)	0.80 (0.44, 1.45)
45-64	0.60 (0.51, 0.71) ^b	0.27 (0.18, 0.41) ^b	0.77 (0.66, 0.91) ^b	0.46 (0.29, 0.73) ^b	0.50 (0.32, 0.78) ^b
≥65	0.62 (0.53, 0.72) ^b	0.62 (0.49, 0.79) ^b	1.07 (1.00, 1.14)	0.93 (0.68, 1.27)	0.62 (0.48, 0.80) ^b
Women					
25-44	0.49 (0.33, 0.73) ^b	0.45 (0.23, 0.85) ^b	0.75 (0.47, 1.20)	0.55 (0.24, 1.25)	0.66 (0.32, 1.39)
45-64	0.65 (0.52, 0.79) ^b	0.31 (0.19, 0.52) ^b	0.80 (0.67, 0.96) ^b	0.52 (0.29, 0.93) ^b	0.52 (0.30, 0.91) ^b
≥65	0.59 (0.49, 0.71) ^b	0.60 (0.46, 0.78) ^b	1.10 (1.03, 1.18) ^b	0.91 (0.63, 1.30)	0.57 (0.42, 0.73) ^b

Note. CI = confidence interval.

^aEstimated by Cox proportional hazards model, with adjustment for education and income.

^bCIs that do not contain 1.00.

Latino preventive health behaviors are somewhat contradictory, however. For example, Latinas (Hispanic women) are less likely to have ever had a Pap test, clinical breast examination, or mammogram than non-Latina Whites.^{30,31} This may be because of lack of health insurance and access to preventive health care.³² Evidence also indicates that health behaviors worsen with acculturation.^{10,33} For example, smoking rates (especially among women) increase with greater acculturation.^{34,35} Moreover, Latinos do not have a mortality advantage for all diseases. Latinos have higher mortality than non-Latino Whites from diabetes, liver disease, homicide (among male Latinos),^{4,5,28} cervical cancer,³ and AIDS.^{27,28} These ratios appear to vary by Latino group and cause of death,^{4,36} but cause-specific mortality has not been systematically examined in Latino subgroups.

If cultural factors, such as health behaviors, operate to produce the lower mortality, might the Latino advantage be evident in international statistics? We examined World Health Organization data to answer this question. In 1990, the all-cause mortality rate (i.e., deaths per 100 000 people in the population) in the United States was 918.4 for males and 812.0 for females.³⁷ Although the rates in Spain³⁷ were comparable—924.5 for males and 788.2 for females (yielding Spain vs United States rate ratios [RRs] of 1.01 for males and 1.03 for females)—to those in the United States, the rates in 3 other Latino countries were lower. The rates³⁸ in Puerto Rico were 892.5 for males and 596.7 for females (yielding Puerto Rico vs United States RRs of 0.97 for males and 0.73 for females); in Cuba, 758.2 for males and 601.0 for females (RRs = 0.83 and 0.74, respectively); and in Mexico, 566.6 for males and 432.0 for females (RRs = 0.62 and 0.53, respectively). Despite the limitations inherent in these cross-national comparisons, including between-country variation in health care, SES, and ethnic composition (e.g., the US data include Whites, Latinos, Blacks, and other groups), these international data are consistent with a cultural explanation of lower Latino mortality.

Finally, a parallel paradoxical finding exists in the literature on infant health. Latinos have lower rates of low birthweight and infant mortality than do non-Latino Whites and other ethnic groups.³⁹⁻⁴³ In general, these studies conclude that psychosocial factors related to Latino culture (e.g., diet, social support, family cohesion) operate as protective factors in infant health.

A systematic test of the hypothesis that cultural factors, especially those involving favorable health behaviors, contribute to Latino health is needed. These tests should examine different causes of death in Latino subgroups and control for demographic differences (e.g.,

SES). If Latinos engage in better health practices, especially relative to risk factors for heart disease and cancer (the most common causes of death for both Latinos and non-Latino Whites), the lower mortality rate may not be paradoxical. The paradox may be that in the United States, the land of opportunity, these health behaviors worsen with acculturation. □

Contributors

A. F. Abraido-Lanza conceptualized, planned, and designed the study; conducted the literature review; analyzed some of the data; and wrote the paper. B. P. Dohrenwend assisted with the study plan and design, contributed to the writing of the manuscript, and provided valued mentoring on all other aspects of the study. D. S. Ng-Mak contributed to the data analytic plan, conducted all the principal analyses, and contributed to the writing of the manuscript. J. B. Turner contributed to the data analytic plan and to the writing of the manuscript. All authors interpreted the data.

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