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Aspirin use and cardiovascular events in social networks

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ABSTRACT

We tested whether friends' and family members' cardiovascular health events and also their own aspirin use are associated with the likelihood that an individual takes aspirin regularly. Analyses were based on longitudinal data on 2724 members of the Framingham Heart Study (based in Massachusetts, U.S.A.) who were linked to friends and family members who were also participants in the same study. Men were more likely to take aspirin if a male friend had recently been taking aspirin, and women were more likely to take aspirin if a brother had recently been taking aspirin. Men were also more likely to take aspirin if a brother recently had a cardiovascular event, and women were more likely to take aspirin if a female friend recently experienced a cardiovascular event. Aspirin use is correlated with the health and behavior of friends and family. These findings add to a growing body of evidence which suggests that behavioral changes that promote cardiovascular health may spread through social networks.

Introduction

A large body of evidence shows that aspirin reduces cardiovascular events for patients with and without histories of cardiovascular disease (CVD) (Berger et al., 2006; Campbell, Smyth, Montalescot, & Steinhubl, 2007; Eidelman, Hebert, Weisman, & Hennekens, 2003; Farley, Dalal, Mostashari, & Frieden, 2006). However, several national studies reveal that aspirin is underutilized (Pignone, Anderson, Binns, Tilson, & Weisman, 2007; Stafford, 2000). Increases in aspirin use have been slow given its efficacy, and rates remain low, particularly among outpatients (Stafford & Radley, 2003). Using the 2003 Behavioral Risk Factor Surveillance Survey, Ajani, Ford, Greenland, Giles, and Mokdad (2006) report adjusted aspirin prevalence rates of 69.3% and 32.7% for individuals with and without CVD. They also find less aspirin use among women than men (adjusted prevalence for women was 34% and for men 38.5%).

Given that aspirin is inexpensive, available without a prescription, and its health benefits have been relatively widely publicized (e.g., industry-initiated advertising campaigns), much of the variation in aspirin use is likely to be determined by factors outside of the clinical setting. While having had a conversation with one's doctor about aspirin is an important determinant of aspirin use in national samples (Brown et al., 2002; Pignone et al., 2007), discrepancies between medical records and self-reports suggest than many people take aspirin on their own initiative without their doctor's knowledge (Brown et al., 2002).

It seems reasonable to suppose that having a member of one's social circle (i.e., an "alter") experience a cardiovascular event and/or begin taking aspirin is likely to affect an individual's (i.e., an "ego") aspirin use. Health behaviors and risk factors (e.g., obesity, smoking) may be "socially contagious," and the chances that one changes his/her own behavior are increased if a member of one's social network recently began behaving differently (e.g., with respect to diet, exercise, smoking, or drinking) (Christakis & Fowler,

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2007, 2008; Rosenquist, Murabito, Fowler, & Christakis, 2010). Aspirin-use may have a comparable dynamic of social diffusion. Having a friend or family member experience a cardiovascular event and/or begin taking aspirin may increase an ego's odds of aspirin-use by increasing his/her awareness of CVD and aspirin prophylaxis. Alters' events and aspirin-use could also raise ego's subjective assessment of personal cardiovascular risk and improve his/her attitudes toward aspirin use. This work departs from prior work in that it evaluates both the similar behaviors in alters (aspirin use) and also events occurring in alters (e.g., cardiovascular illness) with respect to how they affect ego.

Methods

The Framingham Heart Study Social Networks Study

The Massachusetts, U.S.A. Framingham Heart Study (FHS) began in 1948 with an Original Cohort of 5209 adults. In 1971, the FHS added an Offspring Cohort comprised of 5124 adult children of the Original Cohort and their spouses. In 1994, a minority oversample of 508 people known as the "Omni Cohort" was empaneled. Beginning in 2002, 4095 adults having at least one parent in the Offspring Cohort enrolled in the Third Generation Cohort, along with 103 parents of the Third Generation Cohort participants who were not previously enrolled in the Offspring Cohort. As a means of following participants, the FHS collected regular contact information for participants' close friends and family members. Since the FHS cohorts are family-based and participants are drawn primarily from the Framingham, Massachusetts area, many of the friends and family members that were listed as contacts are also participants in FHS. Connecting participants (i.e., egos) at each wave to their contacts who were also participants (i.e., alters) gives researchers longitudinal data on a network of social connections among participants. Combining these network data with data from periodic physical exams and questionnaires allows us to test how alters' recent events and behaviors impact egos.

The Framingham Heart Study protocol is reviewed by the Boston University Medical Center Institutional Review Board and participants signed written informed consent. Our project was additionally reviewed by the Harvard Medical School Institutional Review Board.

Study sample

Longitudinal data for our analysis come from physical exams and questionnaires performed during three-year periods centered at 1985, 1989, 1992, 1997, and 1999. We limit our analysis to egos who are likely candidates for aspirin prophylaxis—that is, women age 55–70 and men ages 45–79. All egos are from the Framingham Offspring Cohort, while alters may be in any of the Framingham cohorts. In this analysis, we include three types of intimate peer relationships: spousal relationships, sibships, and friendships. We select these relationship types because we expect egos to be more sensitive to events/behaviors among alters they identify with and feel close to. An insufficient number of observations and events made it impossible to examine gender-stratified parent–child relationships.

In the data for our analysis, information on egos' and alters' health events, behaviors, and social ties are time-varying across waves. If a respondent lists a friend as a contact in one wave, but not in the next wave, that tie is dissolved and is not included in subsequent waves. If an alter dies between the last and current wave, we include information about the health events leading to his/her death in the current wave, but that tie will be dissolved and is not included in all subsequent waves. Examining ego-alter ties across all waves, 32% of the observations are spousal ties, 58% are sibling ties, and 11% are friendships.

Study variables

The dependent variable for this analysis is a dichotomous indicator for whether ego is taking aspirin on a daily basis at the time of the current wave. The key predictors of interest are whether alter was taking aspirin on a daily basis at the last wave and whether alter had a cardiovascular event between the last and current waves. Specific cardiovascular events included in the alter event measure are: myocardial infarction, angina pectoris, coronary insufficiency, stroke, intermittent claudication, and death from CVD or stroke.

We include a lagged version of the dependent variable as a predictor to adjust for whether ego was taking aspirin at the last wave. We also adjust for whether ego has ever had his/her own cardiovascular event prior to the current wave. The measure of ego's prior events includes: myocardial infarction, angina pectoris, coronary insufficiency, stroke, and intermittent claudication. Other control variables are ego's age, education, marital status, and survey wave.

Statistical analysis

The longitudinal logistic regression model employed in our analysis can be written as:

$$\ln\left(\frac{Y^e_{it}}{1-Y^e_{it}}\right) = \alpha + \beta_1 X^a_{1ir(t,t-1)} + \beta_2 X^a_{2ir(t-1)} + \beta_3 X^e_{3i(t-1)} + \beta_4 X^e_{4it} + \beta_5 X^e_{5it} + \beta_6 X_{6t} + e_{irt}$$

where the superscript e indicates a variable measuring an ego characteristic and a superscript a indicates a variable measuring an alter characteristic. The subscript i refers to individual ego, i, the subscript r refers to relationship, r, with a given alter, and the subscript t refers to a given wave at time t. Y^e_{it} is the dichotomous dependent variable indicating whether ego used aspirin at the current wave. $X^a_{1ir(t,t-1)}$ is a dichotomous variable indicating whether alter experienced a cardiovascular health event between the last wave $(t-1)$ and the current wave (t). $X^a_{2ir(t-1)}$ is a dichotomous variable indicating whether alter was taking aspirin at the last wave. $X^e_{3i(t-1)}$ is a dichotomous measure of whether ego was taking aspirin at the last wave. X^e_{4it} is a dichotomous measure of whether ego had a cardiovascular health event at any time prior to the current wave. X^e_{5it} reflects the set of controls for ego's characteristics (e.g., age, education, marital status). X_{6t} reflects the set of controls for survey wave. And, finally, e_{irt} is an error term specific to each ego-alter pair at a given wave. To account for clustered error terms resulting from ego-alter pairings and multiple observations of the same egos across waves, we use generalized estimating equations with an independent working correlations structure (Hardin & Hibe, 2002).

After presenting a model for all ties combined, we stratify the analysis according to ego's sex, the sex-composition of the tie (i.e., two males, two females, or a male and female), and the type of relationship (i.e., spouses, siblings, and friendships). Aspirin-use is lower among women than men, and evidence of the preventative benefits of aspirin is somewhat more controversial for women than men (Ajani et al., 2006; Mulrow & Pignone, 2005). We further expect that people may be more likely to identify with and take behavioral cues from same-gender alters, and that alter's influence on ego may differ depending on the type of relationship they share (i.e., spouses, siblings, friends).

Table 1
Characteristics of egos and alters in sample.

	Total sample	Male egos	Female egos
Ego Aspirin Use at Current Wave	22.98%	25.45%	19.35%
Alter Aspirin Use at Last Wave	20.03%	18.24%	22.66%
Ego Aspirin Use at Last Wave	19.64%	20.98%	17.67%
Alter CV Event between Last and Current Wave	5.23%	4.29%	6.62%
Ego CV Event Prior to Current Wave	12.88%	15.04%	9.70%
Ego Female	40.46%		
Ego Age (average)[a]	61.279 (7.838)	59.333 (8.339)	64.144 (5.978)
Ego Education			
High School Degree	53.99%	47.89%	62.97%
Associates Degree	8.93%	9.69%	7.81%
Bachelor Degree	15.04%	17.14%	11.97%
Masters/Doctorate Degree	10.74%	15.16%	4.23%
None of the Above	11.30%	10.13%	13.01%
Ego Married	85.60%	90.12%	78.96%
N (Ego-Alter Pair Observations)	19,849	11,818	8031

[a] Standard deviations for ego age in parentheses.

Since siblings are, roughly speaking, equally likely to be male as female, there are comparable numbers of same-sex and mixed-sex sibling pairs and we present estimates separately for sister pairs, brother pairs, and brother–sister pairs. Friendships, on other hand, are much more likely to same-sex than mixed-sex, and we do not have sufficient observations to present separate mixed-sex friendship estimates. We, therefore, present estimates for all friendships combined and then present separate estimates for the subset of same-sex friendships. We conducted all the analysis using STATA SE 10 software.

Results

As shown in Table 1, about 25% of male and 19% of female egos were using aspirin on a daily basis in a given wave. Looking at male and female egos combined in the first column of Table 1, about 20% of their alters were using aspirin daily at the last wave and about 5.2% had a cardiovascular event between the previous and current waves. Table 2 presents odds ratios and 95% confidence intervals from our first regression model including all relationship types and both male and female egos. Older egos, male egos, and egos who had a prior cardiovascular event were more likely to take aspirin regularly. In line with widely documented trends, ego's odds of aspirin use were also higher at more recent waves (Stafford, 2000). Ego's marital status and education, however, were not significantly associated with his/her aspirin use in this sample.

In Table 2, ego's odds of daily aspirin use were 12% higher if alter used aspirin daily at the last wave. On the other hand, there was no significant association between alter's recent cardiovascular events and ego's aspirin use. However, this reflects the overall association for all ego-alter pairs and we expect associations may vary according to ego's gender, relationship type, and the gender composition of the relationship. Tables 3 and 4 replicate the basic model presented in Table 2 stratified according to each of these factors.

In Table 3, male egos' aspirin-use was not associated with their wives' aspirin-use or cardiovascular events. Their aspirin use also did not appear to be sensitive to their sisters' aspirin-use or events. On the other hand, male egos were about 41% more likely to use aspirin if their brothers had a cardiovascular event since the last wave. Brothers' earlier aspirin use, however, was not associated with ego's aspirin use. Men's aspirin-use was about 48% higher if a male friend was using aspirin at the last wave. Men's aspirin-use may also be higher if a male friend had a recent cardiovascular event, but this odds ratio of 1.71 should be interpreted cautiously since the lower bound for the 95% confidence interval is 1.00.

Whereas male egos' aspirin-use was not associated with their sisters' aspirin-use, Table 4 shows that female egos were about 35% more likely to take aspirin if their brother used aspirin at the last wave. Brothers' recent cardiovascular events, however, were not

Table 2
Associations between egos' aspirin use and alters' CV events/aspirin use, odds ratios and 95% confidence intervals for total sample.

	Adjusted odds ratio	95% confidence interval
Alter CV Event between Last and Current Wave	1.08	(0.92, 1.27)
Alter Aspirin Use at Last Wave	1.12	(1.02, 1.24)
Control Variables		
Ego Aspirin Use at Last Wave	7.47	(6.32, 8.82)
Ego CV Event Prior to Current Wave	3.81	(3.11, 4.66)
Ego Age	1.03	(1.02, 1.04)
Ego Female	0.66	(0.57, 0.77)
Ego Education		
Associates Degree	0.97	(0.77, 1.22)
Bachelor Degree	0.92	(0.76, 1.11)
Masters/Doctorate Degree	1.04	(0.83, 1.31)
None of the Above	0.99	(0.79, 1.24)
Ego Married	1.00	(0.82, 1.21)
Survey Wave		
1987–1991	2.25	(1.70, 2.98)
1991–1995	2.05	(1.57, 2.67)
1995–1998	2.38	(1.81, 3.13)
1998–2001	3.30	(2.52, 4.34)
N (Ego-Alter Pair Observations)	19,849	

Table 3
Associations between egos' aspirin use and alters' CV events/aspirin use for male egos, by relationship type.

	Alter's recent cardiovascular event		Alter's previous aspirin use	
	Adjusted odds ratio	95% confidence interval	Adjusted odds ratio	95% confidence interval
Spouses ($N = 3840$)	1.08	(0.68, 1.70)	1.16	(0.93, 1.46)
Opposite-sex Siblings ($N = 3537$)	1.27	(0.79, 2.06)	0.90	(0.69, 1.16)
Same-sex Siblings ($N = 3202$)	1.41	(1.04, 1.93)	1.11	(0.88, 1.40)
All Friends ($N = 1239$)	1.53	(0.90, 2.06)	1.36	(0.96, 1.91)
Same-sex Friends ($N = 1013$)	1.71	(1.00, 2.94)	1.48	(1.03, 2.13)

*Although not included in the interests of space, models for each relationship type include all control variables listed in Table 2 (except Ego Female).

Table 4
Associations between egos' aspirin use and alters' CV events/aspirin use for female egos, by relationship type.

	Alter's recent cardiovascular event		Alter's previous aspirin use	
	Adjusted odds ratio	95% confidence interval	Adjusted odds ratio	95% confidence interval
Spouses ($N = 2482$)	0.93	(0.63, 1.36)	1.30	(1.00, 1.69)
Opposite-sex Siblings ($N = 2257$)	0.67	(0.44, 1.02)	1.35	(1.03, 1.77)
Same-sex Siblings ($N = 2454$)	1.18	(0.62, 2.23)	1.15	(0.88, 1.50)
All Friends ($N = 838$)	1.73	(0.74, 4.05)	0.66	(0.40, 1.11)
Same-sex Friends ($N = 740$)	2.85	(1.27, 6.37)	0.77	(0.45, 1.31)

*Although not included in the interests of space, models for each relationship type include all control variables listed in Table 2 (except Ego Female).

associated with women's aspirin use. Women's odds of aspirin use did not appear to be sensitive to their sisters' aspirin use or health events. Women were more than twice as likely to use aspirin if a female friend recently had a cardiovascular event. However, female friends' recent aspirin use was not associated with women's aspirin use. Women's odds of aspirin use may also be positively associated with their husband's recent aspirin use, however this odds ratio of 1.30 should be interpreted cautiously since the lower bound for the 95% confidence interval is 1.00.

Discussion

Persons in this study were more likely to take aspirin regularly if a friend or family member took aspirin. A growing body of literature shows that behavioral changes that promote cardiovascular health may spread through social networks (Christakis & Fowler, 2007, 2008; Rosenquist et al., 2010). The above results add to this literature by providing preliminary evidence that another important cardiovascular health behavior—regular aspirin use—may also be shaped by how members of one's network behave.

Another contribution of this analysis is the examination of alters' cardiovascular events. This approach has both conceptual and methodological advantages compared to prior work. Conceptually, it broadens the scope of what sorts of inter-personal effects might be relevant to individual and public health. Methodologically, it is advantageous because, when considering the effect of an alter event on an ego behavior, it may reduce concern about confounding (since it is a bit harder to imagine factors that are associated with alter events and ego behaviors than it is to imagine factors that are associated with the same behavior in both egos and alters).

While alters' cardiovascular events were not associated with ego's behavior when looking at average effects among all pairs in Table 2, we did find significant associations among certain subgroups. Men were more likely to take aspirin if their brothers recently had a cardiovascular event, and women were more likely to take aspirin if a same-sex friend recently suffered an event. There has been very little research into how people may learn about their own cardiovascular risk and possibly take cues from their friends or family members' health problems (Khwaja, Sloan, & Chung, 2006). Models and theories of behavioral change posit that health behavior depends on how people perceive their health risk and where they fall on a continuum of "readiness to change" (Prochaska & Velicer, 1997). Having a friend or family member go through an experience like a myocardial infarction or stroke may be an important catalyst on the path toward healthier behaviors and better cardiovascular health.

Because aspirin-use is lower among women than men, and evidence of the benefits of aspirin is somewhat more controversial for women than men (Ajani et al., 2006; Mulrow & Pignone, 2005), we stratified the above models according to ego's sex and the sex-composition of the relationship. While the above analysis does not allow us to draw clear conclusions about sex differences in the spread of aspirin-use through social networks, there are suggestive findings. It is notable, for instance, that only male alters, not female alters, appeared to shape ego's aspirin use. Men's aspirin use was associated with their male friends' aspirin use. Women's aspirin use was associated with their brother's aspirin use. Female alters' (i.e., wives, sisters, female friends) aspirin use, on the other hand, was not significantly associated with ego's aspirin use in any of our stratified models. This greater sensitivity to male alter's aspirin use may result from several different factors including higher rates of aspirin use among men, different perceptions of cardiovascular risk for men and women (Frijling et al., 2004), and gender inequalities in the inter-personal dynamics of ego-alter relationships.

Our analysis also points to possible sex differences in sensitivity to alters' cardiovascular events. Associations between ego's aspirin use and alters' cardiovascular events occurred only within same-sex relationships (i.e., brother pairs for men and same-sex friendships for women). There was no association between the ego's aspirin use and the alter's cardiovascular events within mixed-sex pairs. Although several factors may contribute to this pattern, people probably identify more strongly with, and take more health cues from, people of the same sex.

When interpreting the results of our study, it is important consider the role that subjects' doctors may have played in their behavior. One possible explanation for associations between ego's and alter's aspirin use is that they both have the same physician who encouraged aspirin use. In our study sample, we were able to identify ego-alter pairs who shared the same doctor and adjust our estimates for this potential confounder. Associations between ego's and alter's aspirin use were quite robust to this adjustment and it does not appear that shared doctors can account for our results (see Table S1 in the online data supplement). Unfortunately, our data do not allow us to know whether egos who were influenced by alters' aspirin use involved their doctors in their aspirin use decisions (e.g., when an ego learns of an alter's aspirin use, does she then turn to her physician for advice about aspirin prophylaxis?).

In an effort to focus our study on egos who are likely candidates for aspirin prophylaxis, we analyzed women ages 55–70 and men ages 45–79. We believe this broad, demographically-based definition of an aspirin use risk group is appropriate given that we are examining how people make choices about aspirin use outside of clinical settings. Further, because clinical recommendations regarding regular aspirin use were being developed over the period in our study (i.e., 1971–1998), it is important that we capture a broad segment of the general population.

It should be kept in mind, however, that influences of alters' behaviors and health may operate differently on egos with specific clinical risk factors (e.g., those based on blood pressure, cholesterol, diabetes, etc.). We found consistent results when we replicated our main analysis for the subset of egos with prior cardiovascular events and/or elevated 10-year coronary heart disease risk scores (based on Wilson et al., 1998). However, when we limited the sample further to include only egos with prior cardiovascular events, we no longer found a significant association between egos' and alters' aspirin-use. Interpreting this non-significance is difficult, though, because relatively few egos had prior cardiovascular events, raising concerns about sparse data and large standard errors (these results are presented in the online data supplement). Further research, preferably with larger samples, is needed to know whether individuals at higher risk for cardiovascular disease are more or less sensitive to the health and behaviors of their friends and family. This study makes no suggestions related to clinical guidelines or about who should take regular aspirin doses. Rather, our results document how social networks are correlated with whether or not an individual adopts a regular aspirin regimen, regardless of specific clinical risk factors.

This work has a few notable limitations. It does not randomize individuals into social networks, thus leaving open the possibility that these results may in part reflect homophily-driven selection bias on the basis of unobserved traits (e.g., avidity for drugs) that influence the use of aspirin over time. For instance, we can imagine that individuals with similar tastes, health knowledge, or physical resilience may be more likely to form relationships. Shared leisure time activities, as well as similar sociodemographic positions (e.g., educational backgrounds or professions), may increase the chances that people with underlying tendencies toward aspirin-use meet and form relationships. While observational data can never overcome all concerns about unmeasured confounding, the Framingham

Heart Study Social Networks Study, which is longitudinal and provides several control variables, gives us more leverage on causality than is usually possible with non-experimental data. Most notably, our data allow us to adjust for egos' prior aspirin use and cardiovascular events. Also, as has been widely noted, the Framingham Heart Study sample is somewhat homogenous and does not have a significant percentage of underrepresented minorities.

Because of differences in how questions about aspirin use were asked in earlier and later waves of the Framingham Heart Study, our dependent variable captures daily aspirin use, but does not detect less frequent regular aspirin doses (e.g., taking aspirin every other day). Furthermore, with these data, we can measure egos' aspirin use only every four years or so. Lower levels or shorter-term changes in egos' aspirin use are, therefore, not detected in our study. This may mean that we fail to capture some variation in egos' aspirin use, which would imply our estimates may fall on the conservative side.

Because our dataset captures a limited number of relationship ties, we were unable to stratify the data in certain ways, and there were several questions about heterogeneity across subgroups that we were not able to test. For instance, after stratifying by sex and relationship type, we did not have a sufficient number of observations to test whether associations differed depending on whether ego had cardiovascular disease and/or had taken aspirin previously. It should be kept in mind that the above results reflect average associations for a general population. It remains possible that associations between egos' aspirin use and alters' aspirin use/events may differ when distinguishing between further subgroups. Finally, the analyses comparing results across different types of relationships and exposures are exploratory. We did not have prior hypotheses about effect sizes for different types of relationships or exposures. These results should not be interpreted as evidence of differences in causal effects across groups/exposures. Since there is very little existing research into peer influences in drug-taking behavior, we believe that this type of exploratory analysis provides a useful first step in understanding how networks may shape pharmacotherapy. In this case of an exploratory analysis, it is not clear whether Bonferroni adjustments for multiple hypothesis testing are appropriate; nevertheless, we note that all Bonferroni-adjusted *p*-values in our analysis were greater than 0.05.

Across a broad swathe of behaviors, people are influenced by those around them. Pharmacotherapy is a behavior, and so we should not be surprised by the fact that people's drug-taking behavior is related to the behavior of those around them, and to the events occurring in those around them. Similar to the person who might stop smoking when his friend gets lung cancer, a person whose friend, sibling, or spouse has a myocardial infarction may be more inclined to take aspirin because he/she now has a palpable demonstration of the occurrences the aspirin is intended to prevent, rather than an abstract admonition. Likewise, those whose friends are taking aspirin might follow suit for a variety of reasons, including the basic realization that taking aspirin is not hard at all. People are connected, and so their health is connected.

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Disclosures

Two authors (NAC and JHF) have an equity stake in a company, MedNetworks, that is licensed by Harvard and UCSD to apply some of the ideas embodied in this work related to patient and provider networks.

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Appendix. Supplementary material

Supplementary data related to this article can be found online at doi:10.1016/j.socscimed.2011.12.033.

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