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Evaluating the use of friend or family controls in epidemiologic case-control studies

Charlie Zhong^a, Myles Cockburn^b, Wendy Cozen^b, Jenna Voutsinas^a, James V. Lacey Jr.^a, Jianning Luo^a, Jane Sullivan-Halley^a, Leslie Bernstein^a, and Sophia S. Wang, Ph.D.^{a,*}

^aDepartment of Population Sciences, Beckman Research Institute of the City of Hope, Duarte, CA, United States

^bDivision of Preventive Medicine, University of Southern California and the Keck School of Medicine, Los Angeles, CA, United States

Abstract

Background—Traditional methodologies for identifying and recruiting controls in epidemiologic case-control studies, such as random digit dialing or neighborhood walk, suffer from declining response rates. Here, we revisit the feasibility and comparability of using alternative sources of controls, specifically friend and family controls.

Methods—We recruited from a recently completed case-control study of non-Hodgkin lymphoma (NHL) among women in Los Angeles County where controls from the parent study were ascertained by neighborhood walk. We calculated participation rates and compared questionnaire responses between the friend/family controls and the original matched controls from the parent study.

Results—Of the 182 NHL case patients contacted, 111 (61%) agreed to participate in our feasibility study. 70 (63%) provided contact information for potential friend and/or family member controls. We were able to successfully contact and recruit a friend/family member for 92% of the case patients. This represented 46 friend controls and 54 family controls. Family controls significantly differed from original matched controls by sex and household income. Other characteristics were similar between friend controls and the original study's neighborhood controls.

Conclusion—The apparent comparability of neighborhood controls to friend and family controls among respondents in this study suggests that these alternative methods of control identification can serve as a complementary source of eligible controls in epidemiologic case-control studies.

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*Corresponding author at: Division of Cancer Etiology, Department of Population Sciences, Beckman Research Institute of the City of Hope, 1500 East Duarte Road, Duarte, CA 91010, United States., sowang@coh.org (S.S. Wang).

Declaration of interests

The authors declare they have no conflict of interests.

Conflicts of interest

None.

Authorship contribution

S.S.W., J.V.L. Jr., and L.B. conceived and designed the study; C.Z., J.V., J.L., and J.H. conducted data analysis; S.S.W., J.V.L. Jr., M.C., W.C., C.Z., J.V., and L.B. contributed to data interpretation; all authors contributed to manuscript preparation.

Keywords

Case-control studies; Epidemiologic methods; Non-Hodgkin lymphoma

1. Introduction

A present challenge in conducting epidemiologic case-control studies is the identification and recruitment of suitable controls in a cost-efficient manner. The response rates, and resulting validity, of widely used approaches for recruitment of population-based controls, such as random digit dialing (RDD) and neighborhood walk, have declined. Response rates for RDD have fallen from 75–80% in the 1980s to 55–60% in the 2000s [1–5], largely attributed to the use of caller identification and increasing cellular phone usage [6]. Falling response rates increase the amount of resources required to identify suitable controls, particularly for approaches like neighborhood walk [7] and for some minority populations which require multiple follow-up attempts to ascertain a successful recruit [8,9].

Alternative strategies for identifying and recruiting controls have been proposed. Given the rise in number of households who rely on cell phones as their primary or exclusive mode of communication [10], one alternative strategy is by modifying RDD to incorporate cell phone numbers in place of or in conjunction with traditional landline RDD [11]. However, area codes are not necessarily indicative of geographical location and the use of caller ID may prevent case patients from answering calls from unknown numbers [11,12]. Long-debated alternative methods for epidemiologic recruitment of controls include recruitment of case patients' friends and/or case patients' family members [13–16]. These methods have not been widely employed because of possible limitations, including: (i) potential overmatching of controls by exposures, as friend and family tend to engage in similar behaviors and live in similar areas (should certain exposures be of interest) [17–19] and (ii) potential bias among friend controls towards extroverts whereby introvert case patients may be less inclined to nominate friends and potential bias among who case patients nominate [18]. However, for some scientific questions, the use of such controls could be suitable; specifically, the use of family controls is considered a strength for studies aimed at identifying gene associations [20–23].

In this manuscript, we assess the feasibility of identifying and recruiting family or friend controls for epidemiologic case-control studies. Based on a racially/ethnically diverse 10% sample of female non-Hodgkin lymphoma (NHL) patients in Los Angeles County, we evaluated: (i) the willingness of case patients to provide names of family and/or friends as possible controls; (ii) the willingness of identified friend or family controls to participate in an epidemiologic study and complete a questionnaire; and (iii) the comparability of the questionnaire responses from participating friend or family control to controls recruited by neighborhood walk.

2. Materials and methods

2.1. Parent case-control study

From 2004–2008, we conducted a case-control study of 1006 female B-cell non-Hodgkin lymphomas and 1038 matched controls in Los Angeles County. Case patients were identified by the Los Angeles County Cancer Surveillance Program and controls were recruited by neighborhood walk, matched to case patients within a 5 year age group, race, and socioeconomic status [24]. Specifically, recruiting control participants involved walking neighborhoods and obtaining a census for all households within the series of addresses to be surveyed, until an eligible matched control was identified. This methodology resulted in an 85% response rate among controls. All case patients were interviewed in person and asked detailed questions about their health, including anthropometric characteristics and lifestyle factors.

2.2. Identification of alternative controls

We recontacted 182 living NHL case patients and asked if they were willing to participate in a feasibility study aimed to explore alternative methods for conducting epidemiologic studies. A case patient's willingness to participate upon informed consent was subsequently followed by a request for names and contact information of three friends and three family members, preferably siblings or cousins who were similar in age (within 10 years), race, and sex to the case patient. Case patients were asked to contact their respective controls first and then to provide the potential controls' name and contact information once the potential control gave their permission for the case patient to do so. We attempted to recruit and interview each of the family members and friends for whom we obtained contact information. Upon a potential control's consent to participate, an abbreviated version of parent study questionnaire was administered during a telephone interview.

2.3. Abbreviated questionnaire administration

Among consented controls, the abbreviated questionnaire included targeted areas of interest delineated in Supplementary Table S1 in the online version at DOI: <http://dx.doi.org/10.1016/j.canep.2016.10.007>: (i) demographics, (ii) lifestyle and behavioral characteristics, and (among female respondents) (iii) reproductive characteristics, and (iv) health behavior.

2.4. Analytic methods

First, we calculated the *response rates among contacted case patients* representing their willingness to provide names and contact information for potential friend or family controls defined as the total number of case patients who agreed to participate divided by the total number of case patients contacted. Second, among case patients who consented to participate, we calculated the *response rate for providing the requested information* on respective friend or family controls. This response rate was defined as the total number of case patients who agreed to participate and provided the requested information divided by the total number of case patients who consented to participate in this feasibility study. Third, among identified friends and family members with contact information whom we attempted to recruit, we calculated the respective *response rates of controls that were willing to*

participate in our study. This response rate was defined as the number of contacted controls who agreed to participate and completed our questionnaire divided by the total number of controls contacted. These response rates were calculated overall, by race/ethnicity, and sex (Table 1).

Finally, we compared demographic information and questionnaire responses of highest ranked family control and friend control (to approximate a 1:1 matching method) to the responses from the matched neighborhood matched control that was recruited in the parent case-control study for the case patient. The following criteria were used to rank the family and friend controls: (1) same sex and older than case patient; (2) opposite sex and older; (3) same sex and younger; (4) opposite sex and younger. We compared the frequencies (percent) of the questionnaire responses by calculating the Fisher's exact test for statistical significance using SAS 9.3 (SAS Institute, Cary, NC). These results are shown in Supplementary Table S1 in the online version at DOI: <http://dx.doi.org/10.1016/j.canep.2016.10.007>.

3. Results

3.1. Willingness of case patients to provide names of family and/or friends to serve as potential controls

Of the 182 living NHL case patients contacted, 111 (61%) agreed to participate in our feasibility study (Table 1). Of the 111, 40 (36%) were able to provide names and contact information for potential family member and friend controls, 19 (17%) were only able to provide names and contact information for potential family controls, and 11 (10%) were only able to provide names and contact information for potential friend controls. There were 41 (37%) case patients who consented to participate but were unable to provide names/contact information for friends or family, citing that the potential controls they contacted were unwilling to participate. The 71 (39%) case patients who did not consent to participate cited varying reasons, including: (i) not having told any of their friends or family that they were diagnosed with NHL ($n = 4$); (ii) being willing to participate but not having any friend or family of the same race or general age ($n = 14$); the remaining 37 were soft refusals whereby the case patient verbally agreed to participate but was ultimately unable to be reached. Participation rates were relatively consistent by race/ethnicity.

Of participating case patients, the ability to provide contact information for potential friend controls was highest among Asians (60%) and non-Hispanic Whites (60%), and lowest among Blacks (26%) and Hispanics (29%). The ability to provide contact information for potential family controls was highest among Hispanic (62%) and non-Hispanic Whites (60%) and lowest among Blacks (34%).

3.2. Willingness of identified friend or family controls to participate in an epidemiologic study and complete a questionnaire

In all, we attempted to contact 102 potential friend controls who were identified by 51 NHL case patients. We were able to contact 96 friend controls (for 50 case patients). Of the 96 potential friend controls contacted, 83 controls (from 46 case patients) provided consent and

completed the questionnaire. Of the 46 highest ranked friend controls (matched 1:1 to each case patient); 33 were of the same sex and older, 1 was of the opposite sex and older, 11 were of the same sex and younger, and 1 was of the opposite sex and younger (Table 1). These distributions did not appear to vary across racial/ethnic groups.

Of 99 potential family controls (representing 59 case patients), we successfully contacted 92 potential family controls (representing all 59 case patients), of which 78 consented and completed a questionnaire. These 78 family controls were from 54 case patients, leaving 5 case patients without an identified family control. Of the 54 highest ranked controls, 17 were older siblings or cousins of the same sex, 5 were older siblings or cousins of the opposite sex, 26 were younger siblings or cousins of the same sex, and 6 were younger siblings or cousins of the opposite sex (Table 1).

3.3. Comparability of the questionnaire responses from participating friend or family control and the original control

Among demographic characteristics, statistically significant ($P < 0.05$) differences were observed between family controls and the original controls with respect to sex; the 20% of family controls who were male reflected the difficulty in ascertaining family controls of the same sex for all case patients (see Supplementary Table S1 in the online version at DOI: <http://dx.doi.org/10.1016/j.canep.2016.10.007%20>). Annual household income was also lower among the family controls. Although not statistically significant, family controls were generally younger than the original neighborhood controls. Overall, friend controls appeared similar to the original study's neighborhood controls.

4. Discussion

Results from our feasibility study testing recruitment of different types of controls in a racially/ethnically diverse case-control study of NHL suggest that recruitment of friends and family members as a primary source of controls present a significant challenge for epidemiologic studies. Nevertheless, the high response rate among identified controls makes utilization of friend or family controls a viable method for supplementing other methodologies of control ascertainment. Friend controls in general had a higher response rate than family controls and their responses to the abbreviated questionnaire were closely aligned to those of our original neighborhood controls. However, due to the limited sample size, we cannot exclude the possibility that similarities between friend and family controls with population-based controls may be due to chance. As indicated by Milne and colleagues, another potential consideration for utilizing family controls is in addressing potential bias of higher SES among population-based controls[25]. However, we note that some case patients did not have family members of the same sex, and those that did had greater age differences than their friend controls, potentially introducing corresponding and potentially critical differences in the timing of certain exposures (i.e. DES).

Case patient response rates were similar across racial/ethnic groups; however the ability to provide family or friend controls differed. 40% of the NHL case patients identified as Black provided information regarding friend or family member who could serve as a potential control. Two-thirds of Asian and 73% of non-Hispanic White NHL case patients provided

information on potential controls, which is consistent with other studies[15,26]. We required the participating case patients to contact their potential controls before we made an attempts to do so, likely resulting in our higher response rate among the controls (92%) compared to previously reported efforts (48–70%) [13,19,26,27]. We cannot exclude the possibility of differential participation rates in the general population when men are included [13,15] as our parent study was restricted to female NHL case patients. Because the median age of diagnosis for NHL is 66 years, our ability to identify older family controls was likely diminished [28]. It is possible that higher participation rates might be achieved for disease endpoints with a lower median age of diagnosis.

Prior studies that have used friend or family controls have been conducted primarily within non-Hispanic White populations and have reported that 60–100% of case patients provided controls [13,15,21,26,29–31]. Our response rates for non-Hispanic Whites were comparable to these previous efforts. Although the success of this methodology appeared to be equivalent among Asian-Americans, response rates in our study among Black and Hispanic populations remained low.

Some case patients refused to participate because they had not discussed their NHL diagnoses with friends or family members. The severity of the cancer diagnosis may also impact the willingness to discuss it with others [14]. Several case patients also noted they were unable to provide family members who resided in the United States, which is a particularly important issue to consider when applying this methodology to immigrant populations.

Population-based control recruitment, including the parent study's neighborhood walk methodology, is resource and time intensive. Complementary and, arguably, more convenient methods, such as soliciting information on friends and families to identify appropriate controls, would contribute towards the overall efficiency in finding suitable controls. Specifically, the up-front effort to query friends and family members is an efficient way to create a pool of potentially eligible controls, from which we found in this study to yield higher response rates.

In summary, ascertaining potential friend and family control information from case patients at the time of case recruitment could supplement other methodologies, such as RDD or neighborhood walk, for control identification and recruitment in epidemiologic studies. Continued efforts to identify and improve alternative methods [32,33] for control recruitment in population-based case-control studies are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

| | |
|------------|----------------------|
| RDD | random digit dialing |
| NHL | non-Hodgkin lymphoma |

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Table 1

Response Rates for NHL Case Patients, Highest Rank Matched Friend, and Highest Rank Matched Family Member Willing to Participate in a Health Study.

| | Total | Asians | Blacks | Whites | Non-Hispanic White | Hispanic White |
|--|-------|--------|--------|--------|--------------------|----------------|
| Case Patients | | | | | | |
| Alive and contacted | 182 | 46 | 45 | 91 | 56 | 35 |
| Agreed to Participate | 111 | 30 | 27 | 54 | 33 | 21 |
| | 61% | 65% | 60% | 59% | 59% | 60% |
| Nominated both friends and family members | 40 | 15 | 5 | 20 | 16 | 4 |
| | 36% | 50% | 19% | 37% | 48% | 19% |
| Nominated only friends | 11 | 3 | 2 | 6 | 4 | 2 |
| | 10% | 10% | 7% | 11% | 12% | 10% |
| Nominated only family members | 19 | 2 | 4 | 13 | 4 | 9 |
| | 17% | 7% | 15% | 24% | 12% | 43% |
| Agreed to participate but reported no willing friend or family | 41 | 10 | 16 | 15 | 9 | 6 |
| | 37% | 33% | 59% | 28% | 27% | 29% |
| Refused (includes nonrespondents after initial contact) | 71 | 16 | 18 | 37 | 23 | 14 |
| | 39% | 35% | 40% | 41% | 41% | 40% |
| Highest Rank Friend Controls (1 control per case patient) | | | | | | |
| Attempted to contact | 51 | 18 | 7 | 26 | 20 | 6 |
| Able to contact | 50 | 18 | 7 | 25 | 19 | 6 |
| | 98% | 100% | 100% | 96% | 95% | 100% |
| Completed Questionnaire | 46 | 15 | 7 | 24 | 19 | 5 |
| | 92% | 83% | 100% | 96% | 100% | 83% |
| Older, same sex | 33 | 13 | 5 | 15 | 13 | 2 |
| | 72% | 87% | 71% | 63% | 68% | 40% |
| Older, different sex | 1 | 0 | 0 | 1 | 1 | 0 |
| | 2% | 0% | 0% | 4% | 5% | 0% |
| Younger, same sex | 11 | 2 | 2 | 7 | 5 | 2 |
| | 24% | 13% | 29% | 29% | 26% | 40% |
| Younger, different sex | 1 | 0 | 0 | 1 | 0 | 1 |
| | 2% | 0% | 0% | 4% | 0% | 20% |
| Refused | 4 | 3 | 0 | 1 | 0 | 1 |
| | 8% | 17% | 0% | 4% | 0% | 17% |
| Unable to Contact | 1 | 0 | 0 | 1 | 1 | 0 |
| | 2% | 0% | 0% | 4% | 5% | 0% |
| Highest Rank Family Members (1 control per case patient) | | | | | | |
| Attempted to contact | 59 | 17 | 9 | 33 | 20 | 13 |
| Able to contact | 59 | 17 | 9 | 33 | 20 | 13 |
| | 100% | 100% | 100% | 100% | 100% | 100% |
| Completed Questionnaire | 54 | 16 | 9 | 29 | 20 | 9 |
| | 92% | 94% | 100% | 88% | 100% | 69% |
| Older, same sex sibling | 16 | 2 | 3 | 11 | 5 | 6 |
| | 30% | 13% | 33% | 38% | 25% | 67% |
| Older, same sex cousin | 1 | 0 | 0 | 1 | 1 | 0 |
| | 2% | 0% | 0% | 3% | 5% | 0% |
| Older, opposite sex sibling | 4 | 2 | 0 | 2 | 2 | 0 |
| | 7% | 13% | 0% | 7% | 10% | 0% |
| Older, opposite sex cousin | 1 | 0 | 0 | 1 | 0 | 1 |
| | 2% | 0% | 0% | 3% | 0% | 11% |

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| | Total | Asians | Blacks | Whites | Non-Hispanic White | Hispanic White |
|-------------------------------|--------------|---------------|---------------|---------------|---------------------------|-----------------------|
| Younger, same sex sibling | 22 | 8 (41%) | 4 (50%) | 10 (44%) | 7 (34%) | 3 (33%) |
| Younger, same sex cousin | 5 | 3 (9%) | 1 (19%) | 1 (11%) | 1 (3%) | 0 (0%) |
| Younger, opposite sex sibling | 5 | 1 (9%) | 1 (6%) | 3 (10%) | 3 (15%) | 0 (0%) |
| Younger, opposite sex cousin | 1 | 0 (2%) | 0 (0%) | 1 (3%) | 1 (5%) | 0 (0%) |
| Refused | 4 | 1 (7%) | 0 (0%) | 3 (9%) | 0 (0%) | 3 (23%) |
| Unable to Contact | 0 | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |