



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



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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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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

Abbreviations: RDD, random digit dialing; NHL, non-Hodgkin lymphoma.

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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%20>.

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

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