RESEARCH COMMUNICATION

Characteristics of Hospital Controls According to Willingness to Participate in a Cancer Genetic Epidemiologic Research in China

Lin Li, Min Zhang, CD'Arcy J Holman*

Abstract

Objective: Studies on participants' willingness to be interviewed in-person and donate blood specimens for genetic cancer research are few and most have been conducted in Western countries. Little information exists about the willingness to participate in genetic cancer research in China. Methods: In 2009-2010, 560 hospital controls, matched to incidence cases by age, gender and residency, were randomly selected from outpatients attending the Health Examination Centre at the China Medical University's teaching hospital in Northeast China. Demographic and lifestyle characteristics were measured using a validated questionnaire by face-to-face interview and 5 ml blood samples were collected from consenting participants. A 7-point 'willingness to participate' scale was developed for use by the interviewer to record the levels of ease or difficulty experienced in recruiting each participant. The willingness to participate was compared between different subgroups of participants. Results: The participation rate was 96.1% among the hospital controls. Characteristics associated with willingness to participate were age (≥ 60 years) and tertiary education. Weaker associations with gender and malignancies in first degree relatives were not statistically significant. The factors not strongly or significantly associated with willingness to participate were income, marital status, body mass index, smoking, passive smoking, alcohol consumption, tea drinking, or physical activity. Conclusion: This study suggests that while there is general acceptance of participation in genetic cancer epidemiologic research in China across subgroups of outpatient hospital controls, younger age and education are associated with increased willingness to participate, while lifestyle factors generally had little impact.

Keywords: Genetic cancer research - willingness to participate - case-control study - in-person interview

Asian Pacific J Cancer Prev, **12**, 2323-2328

Introduction

Epidemiologic studies that require participants to respond by being interviewed and providing biologic samples rely on the subject's willingness to participate. Some people may be reluctant to divulge personal information, and numerous other factors can influence participation, including the methods used to contact subjects, the effort required of the participants, and the subjects' opinions of the utility of the study (Brogan, 1980). A few empirical studies conducted in western countries have compared respondents who refused to participate, or those who were intermediate or late responders, with respondents who readily agreed to participate. Their results suggest that persons with particular characteristics are more likely to respond, with the most consistent findings being that reluctant or difficult-to-reach respondents were typically older and less educated than those who readily agreed (Holt et al., 1991; Moorman et al., 1999; Shavers et al., 2002; Voigt et al., 2003; Kjøller et al., 2005).

Public understanding of research may vary according to levels of education and literacy, the existence of a research culture and the extent of debate about science and research in the public domain, as well as cultural variations in the value placed on the individual as distinct from the community (Costello et al., 2000). Little information is available in China on whether those who are keen to participate differ in any particulat characteristics from persons who participate only after a little effort to convince, or from those who are convinced only after a greater effort.

We investigated hospital controls' willingness to participate in a case-control study involving cancer genetic research in China, which included an actual request for blood specimens, in order to determine if willingness to participate is associated with demographic characteristics and lifestyle factors. The results may be useful to other investigators and reviewers of grant applications and journal manuscripts which are concerned about factors associated with participants' willingness to participate in cancer epidemiologic research in China.

*School of Population Health, Medicine, Dentistry and Health Sciences, The University of Western Australia, Perth, Australia *For correspondence: darcy.holman@uwa.edu.au*

Materials and Methods

Study design and participants

The study, as part of three large case-control studies of malignancies, was conducted in Shenyang, the capital city of Liaoning Province, Northeast China. In August 2009 to July 2010, 560 incident cases with a primary diagnosis of leukaemia, or breast cancer, or colorectal cancer were identified from new histopathology and haematology records at the First Hospital of China Medical University, a public teaching hospital with 2,250 beds, around 32,000 inpatients annually and 3,000 outpatients daily. The eligible cases were permanent residents of urban Shenyang aged 18 to 85 years. During the study period, 560 hospital controls were selected from outpatients at the same hospital Most of controls were interviewed within three months after cases were interviewed. A systematic selection process used in our previous studies was adopted for hospital control recruitment (Zhang et al., 2007). They were selected from outpatients who attended the Medical Examination Centre at the First Hospital of China Medical University.

The eligible hospital controls were 'healthy outpatients', meaning they had no disease or history of malignancy, and permanent residents of urban Shenyang. Each hospital control was selected as the first attendee on a given selection day to match the next case on a daily updated list of cases by sex and 5-year age group. The project protocol had received ethics approval upon review by both the Human Research Ethics Committee of The University of Western Australia and the First Hospital of China Medical University authority.

Questionnaire and interview

Subjects were briefed regarding confidentiality and anonymity issues and the general aims of the study to investigate lifestyle factors and genetic biomarkers. An appointment for an interview was made after obtaining the respondent's consent via an initial contact. A face-to-face interview was then conducted by the first author, using a structured questionnaire and usually took 30-40 minutes. The validated and reliable questionnaire, available from the authors upon request, was used to collect the information on: (i) demographic and lifestyle characteristics, e.g., area of residence, education, smoking, alcohol and tea consumption and physical activity; (ii) dietary intake assessed by a food frequency questionnaire (FFQ); and (iii) factors relevant to hormonal status and family history of cancer. The questionnaire was adapted from that used in our previous studies on cancers (Zhang et al., 2002). This instrument was originally modified from one used to study cancers in Shanghai in order to ensure cultural relevance (Ji et al., 1998). The questionnaire was translated into Chinese and checked using back-translation by professional Chinese translators. The internal consistency and reliability of the questionnaire was assessed in a preliminary study and then evaluated by a test-retest. The intraclass correlation coefficients for mean daily intake of tea and alcohol were 0.83 and 0.88 (Zhang et al., 2005). Thus high coefficients for test–retest reliability suggested that the questionnaire may be relied upon in assessing selected demographic characteristics and lifestyle factors (Zhang et al., 2005). A 5 ml blood sample from each consenting participant was requested before the interview.

In addition, a 7-point 'willingness to participate' scale was developed for use by the interviewer to record the levels of ease and difficulty experienced in recruiting each participant. The hospital controls were categorized according to how readily the agreement to participate in the study was obtained, ranging from: 1 extremely difficult, 2 very difficult, 3 relatively difficult, 4 neutral, 5 relatively easy, 6 very easy, to 7 extremely easy. Further explanation of the meanings of these scale categories is given with our results (Tabel 1).

Statistical analysis

All data were checked at the end of each interview for completeness and were coded and analysed using SPSS version 18.0. Participants' self-reported current height in meters and weight in kilograms were used to calculate body mass index (BMI) (weight/height2). Alcohol consumption was assessed using the FFQ. Alcohol consumption was based on habitual diet and a 'reference' recall period was set as one year prior to interview for controls. If there was any recent change in habits, only information on the habits before the change was used in data analysis. The frequency and quantity variables for beer, wine, and liquor were converted into daily intake in ml. Amounts of ethanol ingested were calculated by assuming 10g of ethanol per 285ml of beer, per 100ml of wine, and per 30ml of liquor based on a method used in a previous study (Kropp et al, 2001). Physical activity was expressed in terms of weekly metabolic equivalent task hours (MET hrs/week) (Zhang et al., 2003). MET scores of 6, 4.5, and 2.5 were assigned respectively for vigorous, moderate, and walking activity based on a compendium of physical activities (Ainsworth et al., 2000).

The hospital controls were grouped by willingness to participate in the research into 3 groups: enthusiastic (point 7), moderate (point 4-6) and reluctant (point 1-3) based on the 7-point 'willingness to participate' scale. We emphasise, however, that all participants freely gave consent to participate, albeit reluctant participants were far more cautious than enthusiastic participants and typically asked more questions before making their final decision. Proportions of demographic and lifestyle characteristics of hospital controls according to willingness to participate in the research were compared and statistical significance was assessed by chi-square tests, the p-values calculated were for tests of differences between enthusiastic and moderate groups, and between enthusiastic and reluctant groups.

A separate logistic regression model was run for the enthusiastic and moderate groups, whereby all variables examined were entered into a logistic model to determine which factors independently contributed to the willingness to participate in the study. After adjustment for all other variables analysed, p values were computed for individual variables using Wald's test. The reluctant group was excluded from logistic regression analysis because of the smaller sample size of the group.

Table 1. Distribution of Hospital Controls by Willingness to Participate

7-point willingness to participate*	No. hospital controls (n=560)	Group
7 (Extremely easy)	411 (73.4%)	Enthusiastic (73.4%)
6 (Very easy)	14 (2.5%)	Moderate (20.9%)
5 (Relatively easy)	57 (10.2%)	
4 (Neutral)	46 (8.2%)	
3 (Relatively difficult)	13 (2.3%)	Reluctant (5.7%)
2 (Very difficult)	12 (2.1%)	
1 (Extremely difficult)	7 (1.3%)	

*Measurement of 7-point of willingness to participate; 7, Keen to participate and immediately agreed; 6, Keen to participate and agreed after very little more explanation; 5, Keen to participate and agreed after some more explanation; 4, Neutral at first and agreed after more explanation; 3, Hesitant to participate but agreed after some more explanation; 2, Hesitant to participate but agreed after much more explanation; 1, Hesitant to participate but agreed after very extensive explanation

Results

There were 153 men (27.3%) and 407 women (72.7%) women among 560 hospital controls. Of 583 eligible hospital controls who were approached to participate, interviews were completed for 560 (96.1%). Table 1 presents the distribution of the willingness to participate of hospital controls, showing that most controls were enthusiastic (73.4%) and only 5.7% were reluctant.

Table 2 presents characteristics (%) of hospital controls according to willingness to participate in the research. Characteristics significantly associated with willingness to participate in the research were age, tertiary education and income between enthusiastic and moderate groups. There were not statistically significant differences between enthusiastic and reluctant groups. The average age of the enthusiastic group was younger than in the two other groups. Of the age group ≥ 60 years, there were more participants in the moderate group than in the two other groups, more participants with tertiary education were in the enthusiastic group than in the two other groups, less high income (≥ 2001 per capita, Yuan/month) participants in the moderate group than in the two other groups. Another difference was worth underscoring: more participants who had first degree relatives with malignancies were in the enthusiastic group than in the two other groups although the difference was not statistically significant.

Table 3 presents the adjusted odds ratios and 95% confidence intervals for demographic characteristics and lifestyle factors representing the tendency for each factor to associate independently with status as an enthusiastic participant rather than a moderate participant. Demographic characteristics and lifestyle factors strongly and significantly associated with willingness to participate were age and tertiary education. There were also tendencies for moderate participants to be female and to have no history of malignancy in a first degree relative, although these results were not statistically significant. Little or no inference could be made about willingness to participate with respect to income, marital status, body mass index, smoking, passive smoking, alcohol consumption, tea drinking, or physical activity.

Table 2. Characteristics (%) of Hospital Controls According to Willingness to Participate

Characteristics	Willingness to participate (column %)		
	Enthusiastic (n=411)	Moderate (n=117)	Reluctant (n=32)
Demographic characteristics			
Age (years) Mean	50.6	56.5	54.3
< 60	78.8	59.8	71.9
≥ 60	21.2	40.2	28.1
p*	<0.01	0.36	
Gender			
Male	28.5	23.9	25.0
Female	71.5	76.1	75.0
p*	0.39	0.83	
Tertiary education			
No	75.7	88.0	84.4
Yes	24.3	12.0	15.6
p*	0.01	0.27	
Income (per capita, Yuan/month)			
≤ 2000	75.2	85.5	67.7
≥ 2001	24.8	14.5	32.3
p*	0.03	0.36	
Marital status			
Married	92.9	92.3	90.6
Others	7.1	7.7	9.4
p*	0.81	0.63	
BMI (kg/m^2)			
< 25	71.3	74.4	65.6
≥ 25	28.7	25.6	34.4
p*	0.51	0.50	
Malignancies in first degree relatives			
No	83.0	89.7	90.6
Yes	17.0	10.3	9.4
p*	0.07	0.26	
Lifestyle factors			
Smoking (≥20 packs in lifetime)			
No	82.5	80.3	84.4
Yes	17.5	19.7	15.6
p*	0.60	0.79	
Passive smoking			
No	73.7	74.4	75.0
Yes	26.3	25.6	25.0
p*	0.89	0.87	
Alcohol consumption			
No	63.0	73.5	59.4
Yes	37.0	26.5	40.6
p*	0.05	0.68	
Tea drinking			
No	66.2	70.9	62.5
Yes	33.8	29.1	37.5
p*	0.33	0.67	
Physical activity (MET hrs/week)			
≤ 46.17	49.6	51.3	65.6
> 46.17	50.4	48.7	34.4
p*	0.75	0.12	

*Chi-square test; BMI, body mass index; MET, metabolic equivalent tasks

Discussion

To our knowledge, the present study is the first to investigate the demographic characteristics and lifestyle factors associated with hospital controls' willingness to participate in a genetic cancer case-controls study in

Table 3. Adjusted Odds Ratios and 95% Confidence Intervals for the Odds of Being an Enthusiastic Participant According to Demographic Characteristics and Lifestyle Factors

Characteristics	Enth (n=411)	Mod (n=117)	Adjusted OR[a] (95% CI)	P value
Demographic characteristics				
Age (years) (%)				
< 60	78.8	59.8	1.00[b]	<0.01
≥ 60	21.2	40.2	0.36 (0.22, 0.59)	
Gender				
Male	28.5	23.9	1.00	0.13
Female	71.5	76.1	0.60 (0.31, 1.16)	
Tertiary education				
No	75.7	88.0	1.00	0.02
Yes	24.3	12.0	2.14 (1.11, 4.16)	
Income (per capita, Yuan/month)				
≤ 2000	75.2	85.5	1.00	0.47
≥ 2001	24.8	14.5	1.26 (0.68, 2.33)	
Marital status				
Married	92.9	92.3	1.00	0.77
Others	7.1	7.7	0.89 (0.39, 2.03)	
BMI (kg/m^2)				
< 25	71.3	74.4	1.00	0.30
≥ 25	28.7	25.6	1.30 (0.80, 2.13)	
Malignancies in first degree relatives				
No	83.0	89.7	1.00	0.11
Yes	17.0	10.3	1.73 (0.88, 3.39)	
Lifestyle factors				
Smoking (≥20 packs in lifetime)				
No	82.5	80.3	1.00	0.51
Yes	17.5	19.7	0.79 (0.39, 1.59)	
Passive smoking				
No	73.7	74.4	1.00	0.94
Yes	26.3	25.6	0.98 (0.58, 1.64)	
Alcohol consumption				
No	63.0	73.5	1.00	0.17
Yes	37.0	26.5	1.42 (0.86, 2.37)	
Tea drinking				
No	66.2	70.9	1.00	0.87
Yes	33.8	29.1	1.04 (0.64, 1.71)	
Physical activity (MET hrs/week)				
≤ 46.2	49.6	51.3	1.00	0.22
> 46.2	50.4	48.7	1.32 (0.85, 2.04)	

Enth, Enthusiastic; Mod, moderate; BMI, body mass index; MET, metabolic equivalent tasks; OR: odds ratio; CI, confidence interval; [a]Estimates from logistic regression model, adjusted for all other variables shown in the table; [b]Reference group.

China. The strengths of the study were that a validated and reliable instrument specifically for Chinese was used to collect the information (Zhang et al., 2005), all of the interviews were conducted by a single investigator to avoid intra-interview bias, it included both males and females of all ages, and the representativeness of the sample due to the high response rate 96.1%.

Our qualitative observations during the research suggest that lack of interest, concerns about the time required to participate in the study, as well as a suspicious attitude, were the major issues arising from interactions with reluctant participants and non-participants during hospital controls recruitment. Heilbrun et al. (1991) also found that lack of interest, lack of time, anxiety regarding examination and other non-illness related reasons may be the principal factors associated with nonparticipation during recruitment.

The response rate of hospital controls was higher in our study compared with other studies (McQuillan et al, 2003; Wong et al, 2004; Matsui et al, 2005). A study conducted in Singapore (Wong et al, 2004) showed that only about 49.3% of Singaporeans in the sample were willing to donate blood samples for genetic research. The NHANES American national survey (McQuillan et al, 2003) that collected bio-specimens from a representative sample of the US population showed that in 2000 of the 3680 individuals in the age group selected, 2933 (79.7%) completed the interview, and of these, 2501 (68.0%) agreed to the DNA specimen collection. In a population based cohort study conducted in Japan (Matsui et al, 2005), participation rates in the genetic sub-cohorts were 83-88%, 4.7-9.3% lower than those in the non-genetic sub-cohorts.

The majority of participants in our case-control study were scored as enthusiastic participants. The small number of respondents in the reluctant group limited our ability to find differences between the enthusiastic and reluctant groups. Senior participants (age ≥ 60 years) were more likely to exhibit moderate willingness to participate and, in particular, the older people were generally more conservative towards blood sample donation than younger people. This result was consistent with other studies suggesting that older age was a predictor of a lower participation rate in epidemiologic research (Moorman et al, 1999; Voigt et al, 2003; Kjøller et al, 2005; Chretien et al, 2007).

Our finding that participants with tertiary education were more likely in the enthusiastic group was consistent with the only other similar study, which compared the intermediate- and late-responding control participants with early responders. They found that the intermediate- and late-responding participants were less likely to have ever attended college than early responders (Voigt et al, 2003). Another study found the similar result (Holt et al, 1991). This might arise because the well educated are the group most understanding of the contribution that scientific researches could make to social policy, and are more aware that their participation in medical studies may have an impact on health care resources and other policy issues.

There was tendency towards a difference in willingness to participate with respect to gender in our study, females were more likely to exhibit moderate willingness to participate, albeit not statistically significant. This was consistent with a prior study (Paganini-Hill et al., 1993), however another study found that males were associated with greater required efforts to recruit (Cottler et al., 1987). We did not note any impact of income and marital status on willingness to participate was in general agreement with previous studies (Holt et al., 1991; Voigt et al., 2003). There was no difference on willingness to participate with respect to body mass index in our study, which was consistent with another comparison of the intermediate- and late-responding participants with the early responders (Voigt et al., 2003).

Voigt et al. (2003) found that late-responders were more likely than early responders to be current smokers, Paganini-Hill et al. (1993) also reported that

current smokers were slower to respond and ex-smokers responded more quickly, although the differences were not large. Those results were in contrast with our findings of no differences with respect to smoking. We found that alcohol consumption and physical activity had no impact on willingness to participate, which was consistent with the only similar study suggesting that ever use of alcoholic beverages and recent exercise were similar in all of their study groups (Voigt et al., 2003), also consistent with another prior study (Paganini-Hill et al., 1993). There was no prior report whether passive smoking and tea drinking has any impact on willingness to participate in epidemiologic study.

The perceived aims of the study may be of importance, and the interest in the study topic may improve response. Participants who had first degree relatives with malignancies were more likely in the enthusiastic group, although the difference was not statistically significant. Voigt and colleagues (2003) also observed that early responders were much more likely to have a first- or second-degree relative who had been diagnosed with cancer than intermediate responders, late responders, or initial refusers. A less biased group of participants may be recruited if potential respondents are not aware of the specific disease under study, however, all of the participants in our study were informed about the objectives of the study due to ethical reasons.

Some of the differences between our study and other studies that have compared early respondents with late respondents may be related to the type of interview administered. Two studies used telephone interviews (Cottler et al., 1987; Holt et al., 1991), one used mailed questionnaires (Paganini-Hill et al, 1993), whereas ours used in-person interviews. Another reason may be that most of previous studies were conducted in Western countries (Cottler et al., 1987; Holt et al., 1991; Paganini-Hill et al., 1993; Voigt et al., 2003).

Less-willing participants comprised only 5.7% of hospital controls, if excluding these participants from our study, the response rate would be 90.4%. In practice, if response exceeds 90%, the impact of non response will be minimal (Hartge, 1999). Therefore, excluding them from our study would generally have little effect on the overall distribution of characteristics examined in the hospital controls, Voigt et al. (2003) reached a similar conclusion. When time and funds are scarce, it may be reassuring to know that limiting efforts per recruitment may not seriously compromise the most important results of the study.

In conclusion, the results of this study suggest that while there was general acceptance of participation in genetic cancer epidemiologic research in China across subgroups of outpatient hospital controls, younger age and tertiary education were positively associated with willingness to participate, while lifestyle factors generally had little impact.

Acknowledgements

This work was supported by the National Health and Medical Research Council of Australia project grant (APP ID 572542). L Li was supported by the Australian Postgraduate Award and the University of Western Australia Establishment Award.

The authors acknowledge with gratitude the participation of outpatients in Shenyang. We are grateful for the collaboration received from the participating hospital and the staff; in particular, we would like to thank Professor Liu Yun-peng and Dr Shi Jing of the First Hospital of China Medical University, for their kind assistance. The author(s) declare that they have no competing interests.

References

Ainsworth BE, Haskell WL, Whitt MC, et al (2000). Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc*, **32**, S498-504.

Brogan DR (1980). Non-response in sample surveys. The problem and some solutions. *Phys Ther*, **60**, 1026-32.

Chretien JP, Chu LK, Smith TC, et al (2007). Demographic and occupational predictors of early response to a mailed invitation to enroll in a longitudinal health study. *BMC Med Res Methodol*, **7**, 6-16.

Costello A, Zumla A (2000). Moving to research partnership in developing countries. *BMJ*, **321**, 827-9.

Cottler LB, Zipp JF, Robins LN, et al (1987). Difficult-to-recruit respondents and their effect on prevalence estimates in an epidemiologic survey. *Am J Epidemiol*, **125**, 329-39.

Hartge P (1999). Raising response rates: getting to yes. *Epidemiology*, **10**, 105-7.

Heilbrun LK, Ross PD, Wasnich RD, et al (1991). Characteristics of respondents and nonrespondents in a prospective study of osteoporosis. *J Clin Epidemiol*, **44**, 233-9.

Holt VL, Daling JR, Stergachis A, et al (1991). Results and effect of refusal recontact in a case-control study of ectopic pregnancy. *Epidemiology*, **2**, 375-9.

Ji BT, Chow WH, Yang G, et al (1998). Dietary habits and stomach cancer in Shanghai, China. Int J Cancer, 76, 659-64.

Kjøller M, Thoning H (2005). Characteristics of non-response in the Danish health interview surveys, 1987–1994. *Eur J Public Health*, **15**, 528-35.

Kropp S, Becher H, Nieters A, et al (2001). Low-to-moderate alcohol consumption and breast cancer risk by age 50 years among women in Germany. *Am J Epidemiol*, **154**, 624-34.

Matsui K, Kita Y, Ueshima H (2005). Informed consent, participation in, and withdrawal from a population based cohort study involving genetic analysis. *J Med Ethics*, **31**, 385-92.

McQuillan GM, Porter KS, Agelli M, et al (2003). Consent for genetic research in a general population: The NHANES experience. *Genet Med*, **5**, 35–42.

Moorman PG, Newman B, Millikan RC, et al (1999). Participation rates in a case-control study: the impact of age, race, and race of interviewer. *Ann Epidemiol*, **9**, 188-95.

Paganini-Hill A, Hsu G, Chao A, et al (1993). Comparison of early and late respondents to a postal health survey questionnaire. *Epidemiology*, **4**, 375-9.

Shavers VL, Lynch CF, Burmeister LF (2002). Racial differences in factors that influence the willingness to participate in medical research studies. *Ann Epidemiol*, **12**, 248–56.

Voigt LF, Koepsell TD, Daling JR (2003). Characteristics of telephone survey respondents according to willingness to participate. *Am J Epidemiol*, **157**, 66-73.

Wong ML, Chia KS, Yam WM, et al (2004). Willingness to

donate blood samples for genetic research: a survey from a community in Singapore. *Clin Genet*, **65**, 45-51.
Zhang M, Yang ZY, Binns CW, et al (2002). Diet and ovarian cancer risk: a case-control study in China. *Br J Cancer*, **86**, 712-7.
Zhang M, Lee AH, Binns CW (2003). Physical activity and epithelial ovarian cancer risk: a case-control study in China. *Int J Cancer*, **105**, 838-43.
Zhang M, Binns CW, Lee AH (2005). A quantitative food frequency questionnaire for women in southeast China: development and reproducibility. *Asian Pac J Public Health*, **17**, 29-35.
Zhang M, Holman CDJ, Huang JP, et al (2007). Green tea and the prevention of breast cancer: a case-control study in Southeast China. *Carcinogenesis*, **28**, 1074-8.