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Misclassification of self-reported smoking in adult survivors of childhood cancer

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Abstract

We investigated misclassification rates, sensitivity, and specificity of self-reported cigarette smoking through serum cotinine concentration (liquid chromatography tandem mass spectrometry) among 287 adult survivors of childhood cancer. Overall, 2.5–6.7% and 19.7–36.9% of the self-reported never and past smokers had cotinine levels indicative of active smoking. Sensitivity and specificity of self-reported smoking were 57.5–67.1% and 96.6–99.2%. Misclassification was associated with younger age (OR=3.2; 95% CI=1.4–7.4), male (OR=2.1; 95% CI=1.1–4.0), and past (OR=2.7; 95% CI=1.3–5.8) or current (OR=2.6; 95% CI=1.0–6.6) marijuana use. After adjusting for tobacco-related variables, current marijuana use remained a significant risk for misclassification. Clinicians/researchers should consider bio-verification to measure smoking status among survivors.

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Statistical analysis: Huang, Young

Result interpretation: All authors

Manuscript writing: Huang

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CONFLICTS OF INTEREST

All co-authors confirm that there are no known conflicts of interest.

Keywords

Childhood cancer survivors; cigarette smoking; cotinine; misclassification; tobacco use

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INTRODUCTION

Cigarette smoking is a leading cause of morbidity and mortality (1). Childhood cancer survivors are at increased risk for treatment-related chronic health conditions and premature death than siblings or general populations (2, 3); use of cigarettes can exacerbate this risk. Thus, accurate classification of smoking status will facilitate provision of prevention and cessation approaches to help survivors adopt and maintain optimal health behaviors. Unfortunately, 22% of childhood cancer survivors currently smoke cigarettes (4). Lower smoking prevalence by self-reported methods compared to bio-verification has been observed in different populations (5), but this has not been examined in cancer survivors. This study aimed to evaluate misclassification rates, sensitivity and specificity of self-reported cigarette smoking through serum cotinine verification among adult survivors of childhood cancer who enrolled in St. Jude Lifetime Cohort Study. Additionally, factors associated with misclassifications were investigated.

METHODS

A stratified random sample of 287 survivors aged 18 years was selected using a frequency-matched strategy per age, sex, and race/ethnicity to balance the distributions across three cigarette smoking groups. Participants self-reported cigarette use, socio-demographic and behavioral health information from home via questionnaires distributed approximately one month prior to clinical assessment. The questionnaire contains items querying smoking behaviors, including “Have you smoked at least 100 cigarettes in your entire life?” and “Do you smoke cigarette now?” Consistent with our previous study (6), these two items were used to classify survivors into three subgroups: never smokers (<100 cigarettes over lifetime; n=105), past smokers (100 cigarettes over lifetime, but report no current smoking; n=111), and current smokers (100 cigarettes over lifetime, and report current smoking; n=71). Oversampling the current and past smokers allowed sufficient sample sizes for analysis. Participants provided a research blood sample during medical assessments. Serum cotinine concentrations were quantified by liquid chromatography tandem mass spectrometry analysis (7). Active smoking status was classified by race/ethnicity-specific cotinine thresholds (8). The protocol was approved by institutional review board, and participants provided written informed consent.

Misclassifications were calculated by under- and over-reporting. Under-reporting rate was defined as the percentage of self-reported never and past cigarette smokers who were bio-verified as active smokers. Over-reporting rate was defined as the percentage of self-reported current cigarette smokers who were bio-verified as nonsmokers. Using cotinine assay as the gold standard, validity (sensitivity, specificity, false positive, and false negative) of self-reported smoking was calculated. For current smokers, misclassification and validity were evaluated by light (10 cigarettes per day) and heavy smokers (>10 cigarettes per day) (9).

Bivariate analysis was performed to identify factors associated with misclassifications. Variables with p -value <0.1 were selected into logistic regression analyses (Model 1: combined under- and over-reporting; Models 2a-2c: under-reporting only). Factors under consideration included age at evaluation, sex, race/ethnicity, education, marital status, health insurance status, annual household income, years since diagnosis, received any chemotherapy and/or radiotherapy, social desirability (10), and marijuana use. Marijuana use was self-reported and categorized as never, past and current use. Because smokeless tobacco (e.g., chewing and snuff) (11), combustible tobacco (e.g., cigar and pipe) (12), and secondhand smoke (13) contribute to cotinine concentration, we developed Model 2b by excluding participants who were current users of smokeless tobacco or cigars/pipes, and Model 2c by further excluding those who were exposed to secondhand smoke from Model 2b.

RESULTS

Participants' age at evaluation, sex, and race/ethnicity were balanced among three self-reported smoking groups (p 's >0.05 ; Supplemental Table S1). Based on different models controlling for potential effects of smokeless tobacco, cigar/pipe, and secondhand smoke on misclassifications (Table 1), 2.5–6.7% of the self-reported never smokers and 19.7–36.9% of the self-reported past smokers were classified as active smokers, indicating under-reporting, whereas 4.5–8.5% of the self-reported current smokers were classified as nonsmokers, indicating over-reporting. Without adjusting for tobacco-related variables, sensitivity and specificity for self-reports were 57.5% and 96.6%. After adjustment, sensitivity and specificity were 60.0–67.1% and 98.1–99.2%. For current light smokers, misclassification rate was 14.3%; sensitivity and specificity were 58.1% and 88.2%. For current heavy smokers, misclassification rate was 0%; sensitivity and specificity were 56.9% and 100%.

When combining under- and over-reporting groups (Model 1; Table 2), misclassification was significantly associated with younger age (OR=3.2; 95% CI=1.4–7.4), male sex (OR=2.1; 95% CI=1.1–4.0), and past (OR=2.7; 95% CI=1.3–5.8) or current (OR=2.6; 95% CI=1.0–6.6) marijuana use. Similar results were found in the under-reporting group (Model 2a; Table 2). However, when smokeless tobacco users, cigar/pipe users, and those exposed to secondhand smoke were excluded (Models 2b/2c; Table 2), current marijuana use elevated the odds of misclassification by 5-fold.

DISCUSSION

Up to 7% of self-reported never smokers and 37% of past smokers were bio-verified as active smokers. Our misclassification rates are higher than those in the general population ($<1\%$ in U.S. and 2.6% in England) (14), but are significantly lower than childhood cancer survivors (80%) who participated in a telephone-based cessation intervention (15). This discrepancy may indicate differences in study design (e.g., intervals between survey completion and serum sample collection), confounding by other tobacco-related products, and maladaptive health behaviors (e.g., marijuana use). Interestingly, 4.5–8.5% of current smokers were classified as over-reporting. This does not necessarily indicate an inaccurate cotinine assay, but suggests that (1) because of the time interval from at-home survey

completion to the collection of blood samples in clinic some survivors may have reduced their cigarette use or (2) some survivors were infrequent/sporadic smokers (i.e., “social smokers”) who considered themselves to be a smoker but only used cigarettes in specific situations.

Misclassification was significantly higher in younger survivors who may not identify as a “smoker” secondary to inconsistent smoking patterns or less confidence in reporting smoking status to clinicians. Impressively, marijuana use increased the odds of misclassification. Among participants, 81% of self-reported smokers (including past smokers) had ever used marijuana, which is significantly higher than 58% reported in a national survey (16). Marijuana use by smokers associates with inferior tobacco cessation outcomes (17).

This study has several limitations. First, self-reported smoking and serum data were not uniformly collected together (median intervals=30 days; range=0–185 days). Because cotinine is typically detectable up to 7 days following tobacco exposure (18), longer intervals between survey completion and serum collection may bias misclassification rates, especially for infrequent smokers. Second, the use of modern combustible tobacco (e.g., small cigar and hookah) and electronic nicotine delivery systems (e.g., electronic cigarettes) was not evaluated. There is a particular public health concern about increases in hookah and e-cigarette use. A recent national study found that 2.8% of U.S. cancer survivors are current e-cigarette users, and 6.3% were past users; additionally, 15.6% of the current smokers are current e-cigarette users (19). Another national study suggests that 3.9% of U.S. adults aged 18–40 years are lifetime hookah users (20). Using these alternate tobacco products may elevate cotinine concentration, leading to classification errors. Finally, data of nicotine replacement therapy were not systematically collected from participants whose cotinine values could be elevated.

In conclusion, the validity of self-reported smoking among childhood cancer survivors is poor. Identifying accurate cigarette smoking status for survivors informs clinical decision-making for implementing smoking prevention or cessation strategies. Survivorship-based research utilizing self-reported methods as a primary outcome or a major covariate should be aware that misclassifications could cause misinterpretation of findings. Within the survivorship care setting, while cotinine bio-verification may not be available, the clinical team should consider questions to probe about tobacco use, particularly among survivors who self-report as former smokers, and tailor interventions accordingly. It is also important to collect co-occurring substance use (e.g., marijuana) to supplement the smoking evaluation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviation Key

OR	Odds Ratio
95%CI	95% Confidence Interval

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Table 1

Misclassification rate and validity for the self-reported cigarette smoking method

	Misclassification rate for self-reported cigarette smoking				Validity of self-reported cigarette smoking [†]			
	Never smoker	Past smoker	Current smoker		Sensitivity (true positive)	Specificity (true negative)	False positive	False negative
No exclusion	6.7%	36.9%	8.5%		57.5%	96.6%	3.4%	42.5%
Excluded current smokeless tobacco users and/or current cigar/pipe users	3.2%	25.0%	6.0%		67.1%	98.1%	1.9%	32.9%
Excluded current smokeless tobacco users, current cigar/pipe users, and/or those who were exposed to secondhand smoking	2.5%	19.7%	4.5%		60.0%	99.2%	0.8%	40.0%
Focused on current light smokers (< 10 cigarettes per day) only	–	–	14.3%		58.1%	88.2%	11.8%	41.9%
Focused on current heavy smokers (>10 cigarettes per day) only	–	–	0%		56.9%	100%	0%	43.1%

[†]Use cotinine assay as the gold standard to verify self-reported cigarette smoking status

Table 2

Determinants for the misclassification of self-reported cigarette smoking: multivariable analysis

	Under- or over-reporting	Under-reporting only		
	Model 1	Model 2a	Model 2b [†]	Model 2c [‡]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age at survey completion				
18 – 29.9 years	3.18 ** (1.38, 7.37)	2.96 * (1.25, 7.03)	5.48 * (1.41, 21.35)	4.80 (0.93, 24.75)
30 years	Ref	Ref	Ref	Ref
Sex				
Male	2.05 * (1.05, 4.03)	2.40 * (1.16, 4.97)	1.03 (0.41, 2.60)	1.36 (0.42, 4.41)
Female	Ref	Ref	Ref	Ref
Years since diagnosis				
18 – 19.9 years	Ref	Ref	Ref	Ref
20 – 20.9 years	1.80 (0.81, 4.00)	2.24 (0.97, 5.18)	1.32 (0.42, 4.07)	1.03 (0.27, 4.00)
30 years	1.62 (0.55, 4.76)	1.52 (0.48, 4.76)	2.96 (0.58, 15.13)	1.71 (0.22, 13.29)
Marijuana use				
Never	Ref	Ref	Ref	Ref
Past	2.70 * (1.26, 5.76)	2.89 * (1.27, 6.58)	2.97 (0.97, 9.03)	2.60 (0.67, 10.11)
Current	2.60 * (1.03, 6.57)	3.29 * (1.25, 8.68)	4.56 * (1.21, 17.14)	5.30 * (1.13, 24.86)

[†]Model 2b excluded current smokeless tobacco users and/or current cigar/pipe users;[‡]Model 2c excluded current smokeless tobacco users, current cigar/pipe users, and/or those who were exposed to secondhand smoking.*
p <0.05**
p <0.01