

# Assessment of Tobacco Use in Cancer Survivorship Research Among National Cancer Institute-designated Cancer Centers or Affiliated Universities: A Systematic Review

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This systematic review of the literature examined the role of tobacco use measurement in studies of cancer survivorship performed in the last ten years by National Cancer Institute-designated Cancer Centers or affiliated universities. It was intended to establish the degree to which tobacco use was considered a determining factor. The scientific articles examined for the basis of this review were acquired through PubMed, Google Scholar, references to published papers, and evidence-based papers in the cancer survivorship literature. The exhaustive review found 198 relevant to our aim. Out of the 198 studies examining cancer survivorship found to be published by NCI-designated Cancer Centers or their affiliated hospitals in the last ten years, only 21.2% measured tobacco use as a variable. Given the clear involvement of tobacco use as a risk factor for most cancers, the review determined the variable should be a key metric in epidemiological studies. This indicated the need for increasing inclusion as a key measure in all types of cancer studies, especially those performed by National Cancer Institute-designated cancer centers.

**Keywords:** Cancer survivors, National Cancer Institute-designated cancer centers, tobacco use measurement

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## Introduction

Tobacco use is one of the most prevalent causes of preventable deaths and disability in the US and, in 2004, smoking cost the United States (US) \$193 billion in lost productivity and health care expenses (Association, 2013). Furthermore, smoking is still an extremely prevalent issue in the United States, as 18.1% of adults over 18 years of age were current smokers in 2012, translating to 42.1 million Americans (Agaku, King, & Dube, 2014). Considerable public health funding and efforts have been devoted in the US to reduce exposure to tobacco products in populations and communities. A recent American Association for Cancer Research (AACR) evaluation of 155 National Cancer Institute (NCI) Cooperative Group clinical trials showed that “as few as 29 percent of registered trials assessed any form of tobacco use in patients at enrollment” (Research, 2013). Relatedly, a survey performed by Goldstein et al. reported that only 38 percent of National Cancer Institute-designated cancer centers recorded tobacco use in the medical records as a vital sign (Goldstein, Ripley-Moffitt, Pathman, & Patsakham, 2013). Based on these findings, AACR concluded that there is a widespread disconnect between knowledge of the harm tobacco can cause in humans and its assessment in health outcomes research. In cancer survivorship research, strategies for monitoring and reducing use or exposure to tobacco products and harms are relevant for optimal patient outcomes. Continued smoking after cancer diagnosis can decrease quality of life measures (Garces et al., 2004), as well as increase risk of developing smoking-related secondary primary tumors (Do et al., 2004).

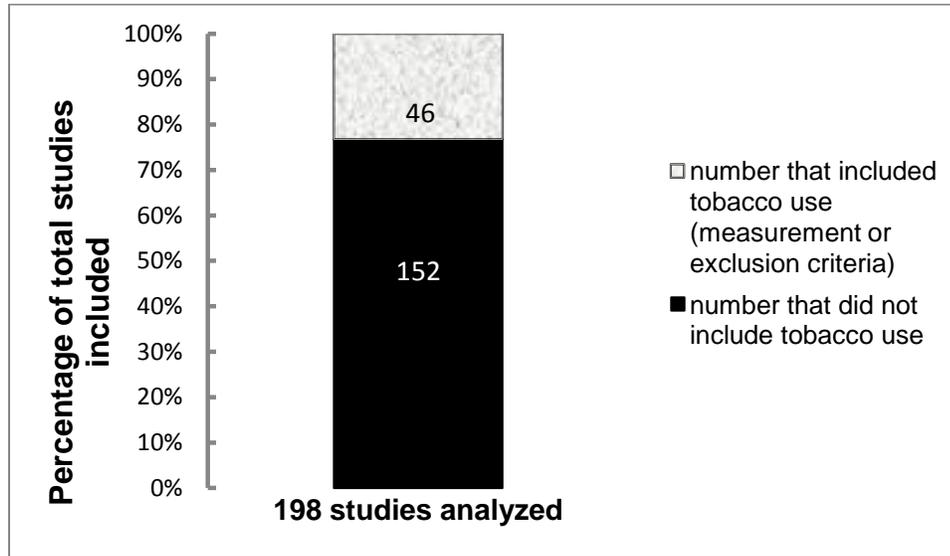
Programmatically, the NCI provides core funding support to cancer centers to achieve the depth and breadth of research in laboratory and population sciences necessary to advance cancer care, reduce cancer burden, and disseminate clinical and public health advances in the communities it serves (Institute, 2015). Given this crucial role, the purpose of this literature review was to examine the extent that tobacco use was a reported measure or outcome in published scientific research on cancer survivorship led or conducted by investigators affiliated with NCI-designated or comprehensive Cancer Centers and/or their affiliated universities. Specifically, this systematic review of the literature had two aims: first, to determine the role of tobacco use measurement in studies with cancer survivorship published in the last ten years by NCI-designated Cancer Centers and, second, to assess whether there was a difference in the inclusion of tobacco use measurement in cancer survivorship studies between the NCI-designated Cancer Centers and the NCI-designated Comprehensive Cancer Centers.

## Results

A total of one hundred and ninety-eight scientific papers met the initial study inclusion criteria and were reviewed to confirm and describe cancer survivorship content related to tobacco use. Of these, forty-two papers (21.2%) reported measurement of tobacco use as a study variable. Four studies, however, measured tobacco use as an exclusion criterion. Thus, Table 1 shows the forty-six papers (23.2%), out of one hundred and ninety-eight that met the criteria of tobacco use measurement.

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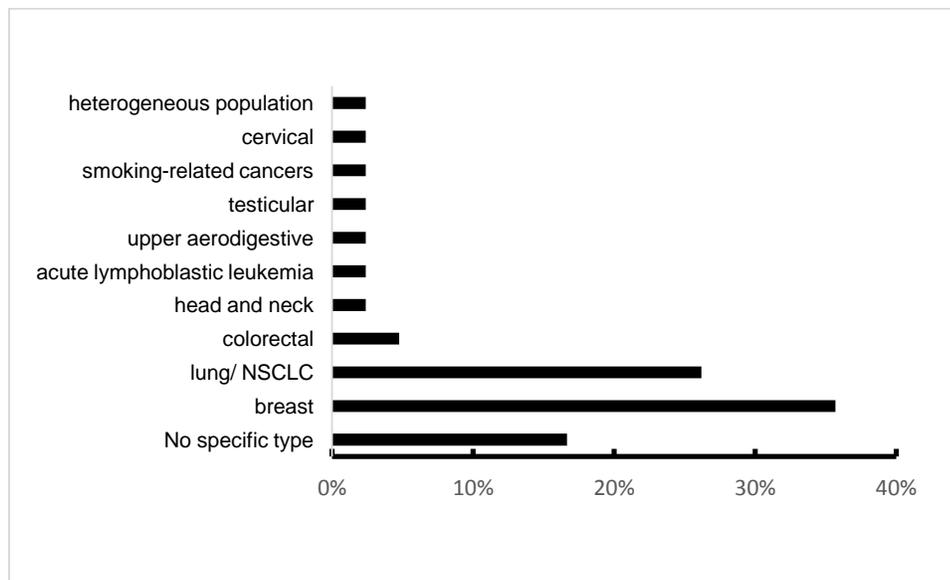
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**Figure 1 – Percentage of analyzed reports that collected tobacco use data.**

In the forty-two papers that measured tobacco use, the majority of these studies measured tobacco use as simply a demographic or medical characteristic, and most simply measured smoking status (e.g., never a smoker, a former

smoker, or a current smoker). Of the forty-two papers that measured tobacco use, there was variability in the type of cancer studied, shown in Figure 2.



**Figure 2 – Distribution of cancer sites among studies measuring tobacco use.**

Seven studies (16.6%) did not have a specific type of cancer studied; 15 studies (35.7%) studied breast cancer; 11 studies (26.8%) studied either lung cancer or non-small cell lung cancer; one study (2.4%) studied head and neck cancers; two (4.8%) studied colorectal cancer; one studied acute

lymphoblastic leukemia; one studied upper aerodigestive cancer; one studied testicular cancer; one studied cervical cancer, one studied a heterogeneous population, and one studied smoking-related cancers.

The percentage of studies measuring tobacco use also varied by cancer site. Of the eleven studies reviewed involving lung cancer patients, 100% measured tobacco use

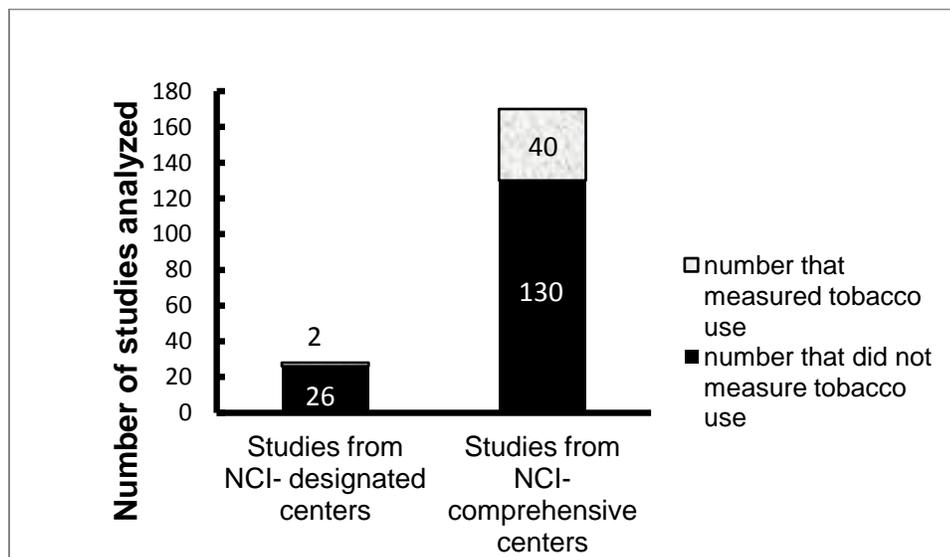
as either a demographic variable or a primary outcome variable. The proportion of the other studies that measured tobacco use by cancer site are shown in Table 1.

**Table 1: Studies Measuring Tobacco by Cancer Site**

Type of Cancer	Number of Studies	Number that measured tobacco	Percentage
Acute lymphoblastic leukemia	2	1	50
No specific cancer site studied	32	7	21.9
Breast	101	15	14.85
Cervical	4	1	25
Colorectal	4	2	50
Lung/NSCLC	11	11	100
Testicular	4	1	25
Other (head and neck, upper aerodigestive, smoking-related cancers, or a heterogeneous population)	4	4	100
Total	198	42	23.2

The studies of cancers that did not measure tobacco use included: breast and prostate; breast, prostate, colorectal, and lymphoma; breast and gynecologic; breast and colorectal; cancer survivors that received hematopoietic stem cell transplantation; cervical and endometrial; ductal carcinoma *in situ*; endometrial; gynecologic; gynecologic and lymphoma; Hodgkin’s Lymphoma; leukemia; non-Hodgkin’s lymphoma; ovarian; prostate; and rectal/anal.

There was also a difference between the NCI-designated Cancer Centers and the NCI-designated Comprehensive Cancer Centers in tobacco use measurement. Figure 3 shows that of the 198 studies selected, 28 (14.1%) were from NCI-designated cancer centers, and 170 (85.9%) were published from NCI-designated comprehensive cancer centers. 7.1% of the designated cancer centers’ studies measured tobacco use, and 23.5% of the comprehensive cancer centers’ studies measured tobacco use.



**Figure 3 – Disparity in reported tobacco use assessment between NCI-designated cancer centers and NCI-designated comprehensive cancer centers.**

Finally, Figure 4 depicts that of the forty-two studies that included tobacco use measurement as a variable, thirty-two, or 78.5%, included tobacco use in the results of the paper,

while 21.5% did not include tobacco use in the results. That is, the latter studies primarily measured tobacco use as a

demographic or medical characteristic and did not include information about tobacco use in the results.

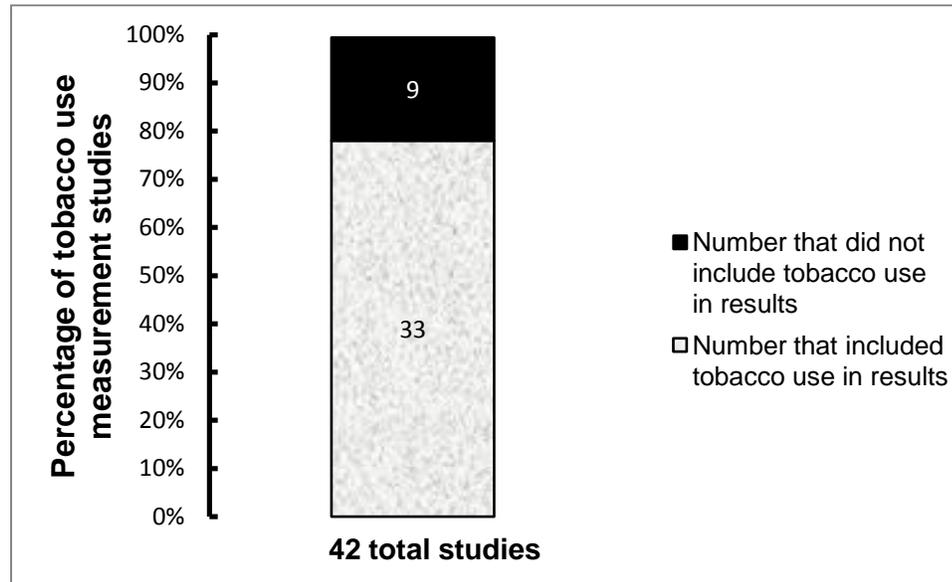


Figure 4 - Percentage of studies that collected tobacco use data that then reported tobacco use in the results.

### Discussion

This systematic literature review illuminated the relatively low prevalence of tobacco use measurement in cancer survivorship studies other than lung cancer. Overall, only 22% of studies found in this systematic review concerning cancer survivors published by National Cancer Institute-designated cancer center investigators measured tobacco use as a variable. This was lower than, but consistent with, the survey findings reported by Goldstein et al that 38% of surveyed NCI-designated cancer centers reported measuring tobacco use as a vital sign in records (Goldstein et al., 2013). While the previous study used data derived from self-report, the present analysis relied on empirical measurement of tobacco use in primary literature. The actual number of survivorship studies that included tobacco use measurement was a simple function of the level of NCI programmatic funding for each tumor site. Most studies focused on breast cancer which receives the largest amount of NCI funding at \$625.0 million in 2011 (Institute, 2013a), followed by lung cancer, which received \$296 million of overall research funding in 2011 (Institute, 2013b). Proportionately, each lung cancer survivorship study found in this review assessed tobacco use versus 18.8% for breast cancer and 50% for colorectal cancer. These results suggested that cross-cutting research priorities, such as promoting survivorship health and well-being, need separate funding initiatives so that less studied cancer diagnoses and patient contexts can be included in this work. This was particularly true given that tobacco smoking was definitively linked to cancers of the colon and the ovary, oral cavity, stomach, liver, pancreas, nasal cavity, larynx, lung, uterine cervix, urinary bladder, kidney, ureter, and bone marrow (Secretan et al., 2009). With these findings, studies that examine the aforementioned cancers should be concerned and interested in

the smoking habits of their patients in order to hopefully improve patient outcomes.

The present results also indicated evidence that a higher proportion of studies from NCI-designated comprehensive cancer centers measured tobacco use than studies from NCI-designated cancer centers - 23.5% compared to 7.1%. This was interesting, yet not a surprising result, because comprehensive cancer centers require a level of qualification for certification than designated centers. Further, NCI-designated comprehensive cancer centers must have an additional component of community- and public health-based initiatives and outreach capabilities. However, it was notable that only 23.5% of studies from the comprehensive cancer centers measured and published tobacco use in their survivorship studies in the last decade. This lack of attention to a chief health risk factor has been echoed in the press release and corresponding paper from the American Association for Cancer Research, and then led the AACR to call for "universal tobacco use assessment and documentation at every patient visit in all clinical cancer settings" (Research, 2013). Comprehensive cancer centers must demonstrate a full range of research and patient care services, including population sciences and cancer control related research (Institute, 2015). Results of this literature search indicated that too few comprehensive centers demonstrated a breadth of research that focused on tobacco use.

Not all of the studies that measured tobacco use as a variable included it in the results section. A possible reason that 21.5 % of the studies did not include tobacco use could be because that it did not appear to use the variable as a covariate when there was a low prevalence of smokers. In the studies that measured tobacco use, there were varying reasons for including use in the results. Some of these studies studied smoking or tobacco use as a primary variable and therefore tobacco use in the results section was logical. Tobacco use

was also included as a medical correlate, but the majority of the studies primarily incorporated tobacco use assessment to control for confounding factors in their different treatment groups. This key finding provided promising evidence for tobacco use measurement in studies, but also highlighted the need to have tobacco use assessment as a larger part of the study than just to control for confounding factors. It was understandable that for some studies, it would not be cost-effective or efficient to do more analysis with tobacco or give out tobacco cessation resources. However, by providing the patients in the studies resources for tobacco cessation, the benefit could be a milestone in cancer prognosis.

This systematic review highlighted the unexpected low percentage of studies that measured tobacco use in cancer survivorship from NCI-designated Cancer Centers or their affiliated universities. However, there were limitations to this review. First, some of these studies examined cancers or treatments that were only vaguely associated to tobacco use. Therefore, some may interpret the results as informative, but only faintly explanatory, and would detract from the feasibility, relevance, or cost-effectiveness of these types of studies. Furthermore, some studies could have measured tobacco use as a variable with no significance in their study and, therefore, findings would not have been reported in their final publication. This limitation could have been enlightening, but considered to skew the analysis and the basic results of this review, artificially decreasing the number that measured tobacco use in this systematic review. Finally, this review had the potential to miss reports, either due to search terms or other unintentional exclusions. However, from this analysis, the strikingly low prevalence of tobacco use measurement in these studies was noteworthy and significant to the literature base.

## Conclusion

With the updated information published about tobacco use linked to 18 different human organ tumor sites, and the policy statement from the American Association for Cancer Research, many more NCI-designated cancer centers, affiliated universities, and other hospital or cancer centers should consider the relevance and critical need to incorporate tobacco use assessment in their clinical trials and their survivorship studies. While it was promising that lung cancer research measured tobacco use the most frequently, there were clearly other cancers linked to tobacco use that did not routinely incorporate this measure in their studies. Smoking has also been shown to be associated with “increased risk of treatment complication, treatment-related toxicity, decreased quality of life, and decreased adherence to treatment” (Toll, Brandon, Gritz, Warren, & Herbst, 2013), as well as an increased risk for secondary cancers (Do et al., 2004). There are myriad reasons, both common and scientific, why tobacco use should be measured and why cancer patients and cancer survivors should be encouraged to quit, regardless of the cancer type. Greater, purposeful steps need to be taken to decrease this large problem in cancer mortality and morbidity. Without solid rationale, the first of these steps could be to measure tobacco use in all clinical trials and survivorship studies. Due to the increase in other forms of tobacco use in recent years, (e-cigarettes, water pipes), measuring all forms of tobacco rather than just smoking status contributes to the

field, the theoretical understanding, and the knowledge base to assess tobacco use. The next step could be to increase the number of studies that refer their patients to tobacco use treatment programs in hospitals and cancer centers around the country, rather than simply controlling for confounding factors with their tobacco use measurements. Tobacco is the “single largest preventable cause of cancer, leading to 30% of all cancer related deaths” (Toll et al., 2013), hence tobacco use measurement should be a key and unexpected variable in cancer clinical trials, cancer survivorship studies, and related epidemiological studies.

## Experimental Procedure

The review of the literature was performed with PubMed and Google Scholar searches. The search terms used were ‘cancer survivorship’, ‘cancer survivors’, ‘quality of life’, ‘tobacco’, and ‘cancer center’. Survivorship or the term “cancer survivor” was defined as including anyone who had been diagnosed with cancer or a focus on the health and life of a person with cancer post treatment until the end of life (Institute, 2014). The latter covers the physical, psychosocial, and economic issues of cancer, beyond the diagnosis and treatment phases and issues related to the ability to obtain health care and follow-up treatment, late effects of treatment, secondary cancers, and quality of life. Cited references of the papers, acquired in this manner, were examined for potentially missed studies, and compared to the most current and available published reviews of the cancer control literature (Harrop, Dean, & Paskett, 2011). Selected for study review were citations of work which met the following initial criteria: (1) published between 2003 and mid-2013; (2) the lead author was affiliated by faculty appointment within an NCI-designated Cancer Center or its affiliate, focused on an aspect of cancer survivorship; and (3) primary data collection (with informed consent) that involved cancer patients who had completed treatment at the time of the study (i.e., chemotherapy, radiation, or surgery). In this systematic review, survivorship was defined as the completion of treatment (whether surgery, chemotherapy, or radiation).

## Data collection

The data extracted from the reviews were the title, first author, year published, and affiliation of first author. Other variables extracted were the designation of the cancer center (Comprehensive or Non-Comprehensive), and whether the study was published from the cancer center or an affiliated university. Other variables measured were the population studied, the type of cancer, the type of study, the purpose of the study, the length of follow-up, the main variables measured, and the results. The variables associated with tobacco use that were extracted included how tobacco use was measured, and if tobacco use was included in the results. Basic Excel graphics and calculations were performed (Microsoft Office 2010).

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