

Original Article

Overcoming challenges of recruiting cancer patients into clinical trials: insights from a randomized trial of app-based smoking cessation interventions

Margarita Santiago-Torres¹, Johann Lee Westmaas², Jamie S Ostroff³, Kristin E Mull¹, Brianna M Sullivan¹, Joseph M Unger¹, Jonathan B Bricker^{1,4}

¹Division of Public Health Sciences, Fred Hutchinson Cancer Center, Seattle, WA, USA; ²American Cancer Society, Atlanta, GA, USA; ³Department of Psychiatry and Behavioral Sciences, Memorial Sloan Kettering, New York, NY, USA; ⁴Department of Psychology, University of Washington, Seattle, WA, USA

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Abstract: Behavioral clinical trials among cancer patients often fail to meet recruitment goals - especially for under-represented groups. Comparing recruitment strategies on participant accrual and cost can inform the use of cost-effective recruitment strategies for enrollment of diverse populations of cancer patients. In this study, we compared social media, internet sites, and clinic-based recruitment on accrual, cost, and characteristics of cancer patients (i.e., sociodemographic, cancer type/stage, and smoking habits) enrolled in a randomized trial of app-based smoking cessation interventions. Fisher's exact tests for categorical variables and analysis of variance for continuous variables were used to compare data between recruitment strategies. In 35 months, 427 cancer patients from 45 US states enrolled in the trial out of 3,936 screened (rate of participation, 10.8%). Social media recruited over eight times the number of enrolled participants (n=340, 79.6%) compared with Internet sites (n=43, 10.1%) and clinics (n=42, 9.8%). Most (80.1%) participants were women, with mean age 52.3 years. About 20.4% of participants were from underrepresented racial/ethnic backgrounds, 23.0% were rural residents, and 23.7% were uninsured. Over 32 cancer types and all cancer stages were represented. Breast cancer was the most common diagnosis (n=129/427, 30.2%), followed by lung cancer (n=96/427, 23.8%). Internet recruitment generated a higher proportion of men (30.2% vs. 26.2% clinics vs. 17.4% social media, $P=.005$). Clinics generated a higher proportion of Hispanic participants (9.5% vs. 7.0% Internet vs. 2.6% social media, $P=.04$) and cancer patients aged 65 and older (28.6% vs. 11.5% social media vs. 4.7% Internet, $P=.01$). Social media recruited a higher proportion of participants with low income (<\$20,000: 39.1% vs. 23.3% Internet vs. 19.0% clinics, $P<.001$), who tended to have later stage cancers (stage IV: 17.4% vs. 14.0% Internet vs. 7.1% clinics, $P=.05$). Cost per randomized participant ranged from \$270 via social media to \$454 via Internet sites to \$2,240 via clinic-based recruitment. In conclusion, social media was the most efficient and cost-effective method for recruiting a quality sample of racially/ethnically, geographically, socio-economically, and clinically diverse sample of cancer patients into a smoking cessation clinical trial. Social media has solid potential for recruiting cancer patients into behavioral clinical trials.

Keywords: Cancer patients, cigarette smoking, digital behavioral interventions, clinical trials, recruitment, smoking cessation, smartphone apps

Introduction

While most cancer patients express a willingness to participate in clinical research, fewer than 1 in 10 cancer patients (between 6.0% and 8.1%) enroll in clinical trials [1-4]. Therefore, clinical intervention trials for cancer patients often fail to meet recruitment targets, resulting in study termination or delay [5-8]. In fact, one

in five clinical trials are terminated for not meeting recruitment targets on time and another third of trials extend their recruitment timeline [9]. Poor accrual of cancer patients is the leading cause of termination or delay, especially among cancer patients from underrepresented groups [10]. While clinical research is crucial in advancing new cancer treatments and improving cancer outcomes and survival, challenges in

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the recruitment and inclusion of diverse populations in cancer randomized clinical trials (RCTs) persist [11].

In a systematic review and meta-analysis, Unger et al., [2] characterized barriers to cancer clinical trial recruitment at multiple levels, including structural, clinical, provider, and patient levels [12]. At the structural level, for example, barriers within the health care system and clinics' lack of prioritizing resources allocated to clinical trials precluded trial participation for the majority of all patients (56%) [13]. At the clinical level, barriers associated with restrictive eligibility criteria precluded trial participation for nearly one quarter of patients (22%). Additional barriers exist at the provider level, for example, there may be lack of engagement and knowledge about trials and limited time that preclude providers from offering trials to their patients. Finally, at the patient level, there are barriers associated with awareness, trust in healthcare systems, lack of transportation, financial assistance, and language barriers, among others.

To address structural, provider, and patient-level barriers to trial participation and increase awareness of and accessibility to clinical trials, one potential approach is to augment the use of clinic-based recruitment strategies with the use of the Internet and social media. Historically, cancer patients relied entirely on their providers to learn about their diagnosis and potential treatments [14]. Presently, the Internet has become a primary source of accessing and disseminating health information [15]. Moreover, as recently as 2020, the vast majority (>80%) of institutional principal or co-principal investigators expressed support for the idea of using social media for trial recruitment; however, few (<25%) actually do [16]. Despite their high population-level reach, very little is known about the potential efficiency and cost-effectiveness of using social media and the Internet to recruit cancer patients into clinical trials compared with more traditional clinic-based strategies (e.g., direct mailings, flyers, provider referrals).

While recommendations to enhance the accrual of cancer patients into clinical trials have been proposed [12, 17], such as diversifying recruitment strategies with online strategies,

very few studies have provided comparative accrual data between strategies used [18]. We are only aware of two RCTs that compared clinic-based to social media recruitment in enrolling cancer survivors to behavioral intervention trials. The first RCT was a rehabilitation clinical trial during the COVID-19 pandemic among breast cancer survivors [19]. The second RCT was a telephone-based smoking cessation intervention for women with a history of cervical neoplasia or cervical cancer [20]. Initially, both trials planned for clinic-based recruitment only, but due to trial recruitment delays, both trials successfully met their recruitment goals on time by augmenting clinic-based recruitment with social media. Although rates of participation were not directly compared between strategies, the use of social media significantly increased the geographic reach of participants enrolled [19, 20]. Empirical data is needed on the effectiveness of diverse strategies to improve participation of cancer patients in behavioral clinical trials, especially among marginalized groups who are underrepresented, to ensure trials are more equitable and findings more generalizable [4].

Our group has previously reported on the use of social media to recruit racially, geographically, and socioeconomically diverse populations of adults in smoking cessation intervention trials delivered remotely via websites and smartphone applications ("apps") [21, 22]. Unknown is whether these strategies are similarly effective for cancer patients. While it may seem logical to focus solely on recruiting cancer patients through social media, our intention was to compare the efficiency, cost, and participant characteristics across multiple recruitment strategies - including social media, Internet sites, and more traditional clinic-based methods. By doing so, we aimed to identify the most effective and cost-efficient approach for enrolling diverse cancer patient populations, particularly given the well-documented challenges in meeting recruitment goal in behavioral trials. Specifically, we aimed to compare recruitment strategies on number of enrollments, cost, and baseline characteristics of cancer patients (all cancer types) enrolled in a behavioral intervention trial of a smartphone app designed to help cancer patients quit smoking [23].

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Materials and methods

Study overview

Quit2Heal is a 12-month, two-arm, parallel group RCT designed to compare the Quit2Heal smartphone app specifically developed for cancer patients who smoke to the QuitGuide app, which is based on US Clinical Practice Guidelines. The planned enrollment goal was 422 patients. The details of the trial have been previously published [23]. The trial was pre-registered on ClinicalTrials.gov (Identifier: NCT04409236; trial dates, July 2021 to May 2026). All study activities were approved by the Institutional Review Board at the Fred Hutchinson Cancer Center (Protocol number: IR-10432/RG1007577). Enrollment was completed in June 2024. Data collection on intervention engagement and outcomes is ongoing.

Inclusion criteria

Interested individuals were eligible if they (1) were 18 years and older; (2) had a cancer diagnosis (all types and stages of cancer) within the past 24 months or were receiving or planning to receive cancer treatment within three months of enrollment; (3) smoked a cigarette (even a puff) in the past 30 days; (4) were interested in learning skills to quit smoking; (5) were willing to be randomly assigned to either app; (6) lived in the US and were planning to remain in the US for the next 12 months; (7) had daily access to their own smartphone; (8) had knowledge on how to download an app; (9) were able to read English; (10) were not currently (i.e., within past 30 days) using other smoking cessation interventions; (11) had never participated in our prior research trials; (12) had never used the National Cancer Institute (NCI)'s QuitGuide app; (13) were willing to complete a follow-up survey at 3-month, 6-month, and 12-month follow-ups; and (14) were willing to provide contact information: email, phone number(s), and mailing address.

Exclusion criteria

Interested individuals were excluded if they (1) used other non-pharmacological smoking cessation interventions within the last 30 days; (2) previously participated in our trials; (3) used

the NCI's QuitGuide app in the past; (4) were unwilling to complete follow-up surveys; and (5) declined to provide contact information.

Recruitment methods

Recruitment methods were designed to achieve a broad representation of cancer patients with racial/ethnic, geographic, and clinical diversity. Main recruitment methods included (1) limiting recruitment to no more than 70% non-Hispanic White individuals; (2) using diverse recruitment strategies including social media, Internet sites, clinic-based (i.e., mailing and provider referrals), and traditional recruitment (i.e., radio); (3) developing tailored recruitment materials; (4) collaborating with NCI-designated comprehensive cancer centers and non-profit cancer organizations to advertise the trial via their clinics, websites, and social media outlets; and (5) hiring a vendor (i.e., Targeted Performance Partners[®]) to contact cancer centers in the ten states with high smoking rates (i.e., Alabama, Arkansas, Indiana, Kentucky, Louisiana, Missouri, Mississippi, Ohio, Tennessee, West Virginia) and recruit physicians and staff to refer patients and distribute flyers in their clinics.

The development of tailored recruitment materials included the design of social media advertisement (ad), flyers and brochures, press releases, and registration website (Quit2Heal.org) content tailored to cancer patients who smoke. In addition, we continuously monitored participant accrual throughout the trial and made refinements accordingly as needed, including (1) expanding the eligibility criteria with regards to cancer treatment timeline (i.e., initial criteria were being diagnosed within 12 months or currently receiving treatment) and (2) reducing the number of quiz questions in the screening survey. The quiz questions were designed to confirm participants' understanding of study requirements. For example, 'You may be randomly selected to take a test to verify your smoking status. The testing device measures your saliva. Just to make sure you understand, what does the testing device measure?' With response options, (a) your breath, (b) your saliva, (c) your blood, (d) your urine. Below, we describe the primary recruitment strategies and methods used (**Table 1**).

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Table 1. Main recruitment strategies and methods^a

Strategy	Method
Social media	Tailored social media ads with selected characteristics intended to reach cancer patients who smoke and want to quit smoking.
Internet sites	Tailored advertisement at the American Cancer Society and Fred Hutchinson Cancer Center main pages and posting in their social media outlets (e.g., Facebook, Instagram, Twitter).
Clinics	Provider referrals, in-clinic (tailored flyers), and remote recruitment (direct mailings, calls, and emails) to cancer patients identified via electronic health records.
Traditional	Paid radio advertisement.

^aRefer to **Table 6** for a complete list.

Recruitment strategies

Social media: Social media recruitment strategy included Facebook and Instagram paid ads. Recruitment methods used for the social media ads included: (a) tailored ads directing potential participants to the registration website (**Figure 1A**); (b) increasing the variety of social media ads; (c) including still images, single and carousel ads, and video ads with and without sound (Refer to multimedia to watch [Supplementary Video](#)); and (d) monitoring ad campaigns and increasing the daily budget on the most successful ads. Social media tailored recruitment methods also included selecting a wide range of cancer care settings and organizations, professional associations, and magazines (e.g., American Cancer Society, Memorial Sloan Kettering Cancer Center, Mayo Clinic, MD Anderson Cancer Center, Breast Cancer Awareness by Greater Good Charities, LIVESTRONG.com), along with characteristics associated with smoking and smoking control initiatives (e.g., cigarette brands, smoking/no smoking).

We also ran ads on Google and YouTube but discontinued them after the ads failed to result in any randomizations after a few months. Although TikTok was reported by participants as their recruitment source, the study did not post ads on this site because of organizational policy at the Fred Hutchinson Cancer Center.

Internet sites: Several Internet sites were used to advertise the trial, including posting at a non-profit cancer organization (American Cancer Society (ACS)'s Cancer.org) and the Fred Hutchinson Cancer Center in Seattle, WA (FredHutch.org) webpages (**Figure 1B** and **1C**). Recruitment methods used for the advertisement at ACS included: (a) prominent placement of the study on Cancer.org, including the main

landing page, (b) releasing a press statement about the study, (c) leveraging ACS resources for social media campaigns and posting weekly on the ACS's Facebook page, which has over 1.1 million followers, (d) distributing flyers at Hope lodging houses, and (e) integrating study promotion into ACS events like the "Great American Smoke out" and "Relay for Life".

Recruitment methods used for the advertisement at Fred Hutch included: (a) social media ad campaigns, primarily on Facebook and Instagram (**Figure 1C**), but also with brief campaigns on Google and YouTube, (b) distributing flyers at Fred Hutch clinics and patient lodging houses, (c) referrals through the Fred Hutch's Tobacco Treatment Program, and (d) presentations to Fred Hutch medical providers. The study registration website was also accessible via online search engines (e.g., Google, Safari).

Clinic-based recruitment: Clinic-based recruitment was primarily conducted through health-care providers and staff at Memorial Sloan Kettering (MSK) Cancer Center in New York city, New York. In-clinic recruitment methods included study flyers, brochures, ticker-tape messages on waiting room video screens, and direct referrals by providers (**Figure 1D**). Clinic-based remote recruitment methods included proactive calls to approximately 1,800 patients, direct mailing of flyers to 2,236 patients, and emails sent to 7,844 eligible patients identified by providers and electronic health records.

In addition, fourteen other hospitals and medical institutions promoted the study to their patients. Between June and July 2022, TPP (hired vendor) made 500 calls, reaching 71 clinics. Of those, twelve agreed to promote the study to their patients across seven US states (Indiana, Louisiana, Missouri, Mississippi, Ohio,

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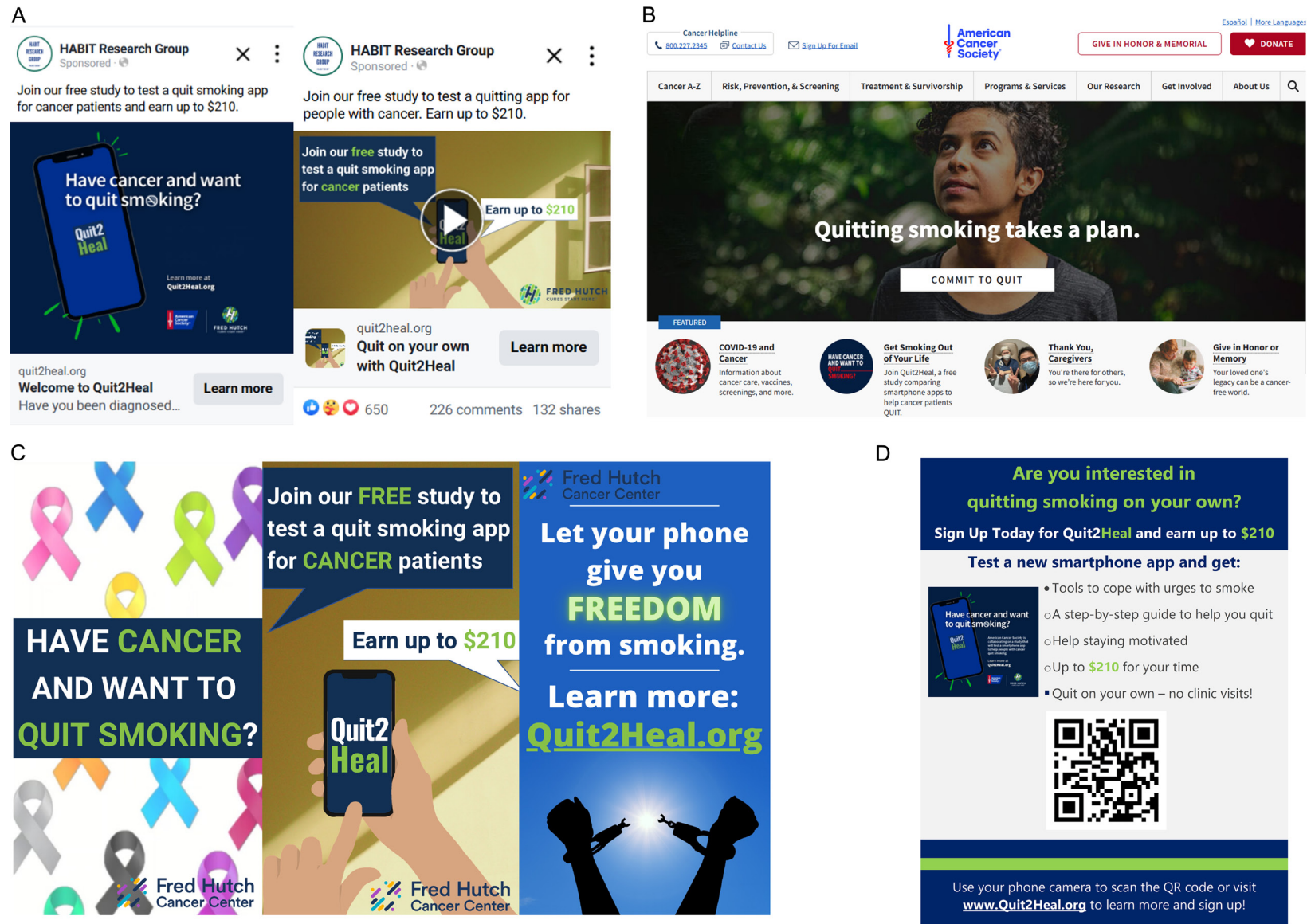


Figure 1. Recruitment ads. A. Facebook still image and video ad (Refer to multimedia to watch [Supplementary Video](#)). B. Internet site ads (ACS main page). C. Internet site ads (Fred Hutch). D. Study Flyer.

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Tennessee, West Virginia), 40 requested more information, and 20 declined (of those 20, 19 do not participate in referral programs for clinical trials and one did not believe they would be able to make any successful referrals). Two additional institutions (Roswell Park in Buffalo, New York, and University of Kansas Medical Center in Kansas City, Missouri) advertised the trial by mailing over 4,000 study flyers to potential participants.

Finally, the study was advertised via the C31 Listserv, a listserv for the NCI's Cancer Center Cessation Initiative. The initiative reaches tobacco control researchers and clinicians at 52 US cancer centers and is dedicated to increasing access to tobacco cessation interventions to cancer patients. The posting via the C31 Listserv consisted of a description of the study with a link to the registration website and offer to provide study flyers with quick response (QR) codes for distribution at clinics in June 2022.

Traditional recruitment: iHeartMedia® was hired for a four-week digital radio advertising campaign focusing on areas with high cancer and smoking rates (i.e., Detroit, Cleveland, Memphis, Milwaukee, Philadelphia, Baltimore, Tulsa, Oklahoma City, Las Vegas, and Tampa) in January of 2023. In addition, the Principal Investigator (PI) of the trial, Dr. Bricker, appeared in a news segment on Seattle's King 5 channel promoting the study. Although newspaper was reported by participants as another recruitment source, the study did not post ads via this outlet.

Enrollment

All recruitment strategies directed individuals to the Quit2Heal.org registration website which provided information about the study, a brief video, information about the study team and academic institutions (i.e., Fred Hutch, MSK), frequently asked questions (FAQs), and access to a secured portal to the screening survey to determine eligibility. In addition to determining eligibility criteria, participants were asked how they found out about the study (i.e., social media, Internet, and clinics). Eligible individuals were then directed to complete the consent form and baseline survey. The trial adhered to our established digital intervention trial enrollment protocols detailed elsewhere [21]. Those who were eligible and provided their email

address received an immediate invitation to complete a secured online survey for informed consent and the study baseline survey, with two reminders sent within 14 days, when necessary. To maintain trial integrity, we implemented robust fraud detection and data quality monitoring at multiple states of the trial. Details of these processes have been previously published [23]. Refer to **Table 6** for a complete list of recruitment strategies and methods.

Baseline data collection

The baseline survey collected data on socio-demographic characteristics (e.g., income, education, zip code), cancer-related information (e.g., diagnosis, stage, depression [24], and anxiety [25]), smoking behaviors (e.g., duration of smoking, confidence in quitting), and alcohol consumption (e.g., daily count).

Statistical analysis

Differences in baseline socio-demographic characteristics, cancer-related information, smoking behaviors, and alcohol consumption between recruitment strategies were assessed using Fisher's exact test for categorical variables and analysis of variance for continuous variables. All analyses were completed in R version 4.2.3. [26], using libraries 'arsenal' [27] for statistical summaries, and 'zipcodeR' [28] and 'ggplot2' [29] for mapping participant zip codes.

Results

Recruitment and enrollment

Over the span of 35 months, 427 cancer patients from 45 US states were enrolled in the trial. The number of screened, eligible, and consented participants by recruitment strategy are shown in **Figure 2**. Of a total of 3936 individuals screened, 427 were enrolled in the trial, resulting in a participation rate of 10.8% (427/3936). Of the individuals screened, 3291 (83.6%) were recruited via social media, 374 (9.5%) via Internet sites, and 255 (6.5%) via clinics. About half of those screened were deemed eligible to participate across all recruitment strategies (53.5% social media, 49.2% Internet, 50.2% clinics). The main reasons for ineligibility were no cancer diagnosis, over two

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years since cancer diagnosis or no planned treatment within 3 months and failing the quiz demonstrating comprehension of study requirements.

Beyond ineligibility, the main reasons for not consenting to participate included not completing the consent process within the designated timeframe and post-screening fraud check failure. These fraud checks were used at various points during the enrollment process and were intended to decrease the likelihood of fraudulent participation such as duplicate enrollments and changing responses to become eligible. Antifraud measures included reviewing internet protocol addresses for duplicates, Completely Automated Public Turing test to tell Computers and Humans Apart (CAPTCHA) authentication and reviewing survey logs for suspicious response times. Staff contacted individuals with suspicious responses to confirm their information.

A total of 747 individuals consented to participate. Of those, 615 were recruited via social media (n=615/747, 82.3%), 69 via clinics (n=69/747, 9.2%), and 61 via Internet sites (n=61/747, 8.2%). Among consented participants, 320 (42.8%) were deemed ineligible after consent, with the main reasons for ineligibility including failing the post-baseline survey fraud check (n=130/747, 17.4%), not completing the baseline survey (102/747, 13.7%), and duplicate households (39/747, 5.2%).

Accrual by recruitment strategy

Social media recruited the overwhelming majority of randomized participants (n=340; 79.6%), followed by Internet sites (n=43; 10.1%) and clinics (n=42; 9.8%) (**Table 2**). In absolute numbers, social media recruited over eight times the number of enrolled participants compared to Internet- and clinic-based recruitment. Facebook advertising was the primary source of social media recruitment (n=337; 78.9% of the total sample) and transitioning from the use of still images, single, and carousel ads to video ads was a key modification (Refer to multimedia to watch the [Supplementary Video](#)). This change led to a 5-fold enrollment rate increase, from approximately 4 to 20 cancer patients enrolled per month. American Cancer Society was the primary source of Internet-based recruitment (n=28; 6.6% of the total sample);

and Memorial Sloan Kettering Cancer Center was the primary source of clinic-based recruitment (n=24; 5.6% of the total sample). Finally, traditional recruitment (e.g., radio ads) did not generate any cancer patients enrolled in the trial.

Cost per randomized participant by recruitment strategy

Social media: The total cost of Facebook and Instagram paid ads was \$91,765 for four campaigns over three years (June 2021 to May 2024), which resulted in 340 randomizations. The cost per randomized participant was \$270.

Internet sites: Most of the Internet-based recruitment strategies (Fred Hutch, online search engines) were free of cost except for the recruitment costs incurred by the American Cancer Society (ACS). These included personnel time for the creation and posting of recruitment images on internal ACS social media outlets (Facebook, Instagram, Twitter) and paid external Facebook ads, advertising the trial on various tobacco or cancer-related webpages and special events (e.g., Relay for Life), and distributing flyers at Hope Lodges. These efforts resulted in 43 total randomizations at a total cost of \$19,593, or \$454 per randomized participant.

Clinic-based recruitment: The total cost of clinic-based recruitment efforts at Memorial Sloan Kettering Cancer Center, which included personnel time for screening and calling eligible patients, emailing recruitment materials and direct mailing of flyers was \$86,736, which resulted in 24 total randomizations. An additional \$1,633 were spent to mail recruitment materials to other hospitals or medical institutions and \$5,700 were spent to hire a vendor for clinic and provider outreach (i.e., TPP), which entailed making 500 calls between June and July of 2022. Overall, the total cost of clinic-based recruitment was \$94,069, which resulted in 42 total randomizations. The total cost per randomized participant recruited via clinics was \$2,240.

Radio: The total cost of radio advertisement at iHeartMedia was \$7,500 for two targeted radio ads in 15 cities for a month (January 2023), resulting in zero randomizations.

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Table 2. Reported recruitment strategy and accrual of randomized participants

	All screened		Randomized	
	N	%	N	%
Recruitment source	3936	100%	427	10.8%
<i>Social media</i>				
1. Facebook	3218	81.8%	337	78.9%
2. Instagram	28	0.7%	1	0.2%
3. YouTube	19	0.5%	1	0.2%
4. TikTok	26	0.7%	1	0.2%
	3291	83.6%	340	79.6%
<i>Internet sites</i>				
5. American Cancer Society	206	5.2%	28	6.6%
6. Google	58	1.5%	7	1.6%
7. Fredhutch.org	27	0.7%	4	0.9%
8. Quit2Heal.org	54	1.4%	2	0.5%
9. All other websites	29	0.7%	2	0.5%
	374	9.5%	43	10.1%
<i>Clinic-based recruitment</i>				
10. Memorial Sloan Kettering	127	3.2%	24	5.6%
11. Other hospital or medical institution	126	3.2%	18	4.2%
12. Listserv	2	0.1%	0	0.0%
	255	6.5%	42	9.8%
<i>Traditional recruitment</i>				
13. Radio	3	0.1%	0	0.0%
14. Newspaper	2	0.1%	0	0.0%
15. Television	2	0.1%	0	0.0%
	7	0.2%	0	0.0%
<i>Unknown source</i>	9	0.2%	2	0.5%
TOTAL				100%

Geographical reach

The trial enrolled a geographically diverse sample of cancer patients recruited nationwide (45 out of 50 US states, excluding Alaska, Hawaii, North Dakota, South Dakota, and Maine) (**Figure 3**). Social media recruitment generated the highest geographic diversity with 45 US states represented, followed by Internet sites (28 US states), and clinics (13 US states). Approximately 23.0% of participants lived in a rural area, with Internet sites recruiting the highest proportion of participants living in rural areas (25.6%), followed by social media (24.1%), and clinics (9.5%) (**Table 3**).

Socio-demographics characteristics of participants by recruitment strategy

Overall, participants were predominantly women (80.1%), mean age 52.3 (SD, 10.8) years, and 20.4% had underrepresented racial/ethnic

backgrounds (**Table 3**). About a third of the sample had a college degree or higher education (35.5%), were employed (33.5%), and had annual incomes of \$55,000 or higher (35.4%). However, about two-thirds (66.5%) of the sample were either unemployed, disabled, or out of the labor force.

Compared to social media and Internet recruitment, clinic-based recruitment generated the highest proportion of Hispanic participants (9.5% vs. 2.6% social media vs. 7.0% Internet, $P=.04$) and cancer patients aged 65 and older (28.6% vs. 11.5% social media vs. 4.7% Internet; $P=.01$). Internet recruitment generated the highest proportion of men (30.2% vs. 26.2% clinics vs. 17.4% social media, $P=.005$). Social media-recruited participants were more likely to have lower income (<\$20,000: 39.1% vs. 23.3% Internet vs. 19.0% clinics, $P<.001$) and be unemployed (22.1% vs. 16.3% Internet vs. 14.3% clinics, $P=.006$).

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Table 3. Socio-demographic characteristics of participants by recruitment strategy

Characteristic	n	Overall ^a n=427	Recruitment source			P value
			Social media n=340 (79.6%)	Internet sites n=43 (10.1%)	Clinic n=42 (9.8%)	
Age, years, mean (SD)	427	52.3 (10.8)	51.9 (10.7)	50.7 (9.5)	57.8 (11.3)	.002
Age, years, no. (%)	427					.01
18-24		2 (0.5%)	2 (0.6%)	0 (0.0%)	0 (0.0%)	
25-44		(23.8%)	81 (23.8%)	15 (34.9%)	5 (11.9%)	
45-64		269 (63.3%)	218 (64.1%)	26 (60.5%)	25 (59.5%)	
>65		53 (12.5%)	39 (11.5%)	2 (4.7%)	12 (28.6%)	
Gender, no. (%)	427					.005
Male		84 (19.7%)	59 (17.4%)	13 (30.2%)	11 (26.2%)	
Female		342 (80.1%)	281 (82.6%)	30 (69.8%)	30 (71.4%)	
Nonbinary		1 (0.2%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	
Race, no. (%)	427					.30
American Indian or Alaska Native		4 (0.9%)	3 (0.9%)	1 (2.3%)	0 (0.0%)	
Asian		4 (0.9%)	4 (1.2%)	0 (0.0%)	0 (0.0%)	
Black or African American		55 (12.9%)	49 (14.4%)	4 (9.3%)	2 (4.8%)	
Native Hawaiian or Pacific Islander		0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
White		349 (81.7%)	272 (80.0%)	35 (81.4%)	40 (95.2%)	
Multiracial		13 (3.0%)	11 (3.2%)	2 (4.7%)	0 (0.0%)	
Unknown race		2 (0.5%)	1 (0.3%)	1 (2.3%)	0 (0.0%)	
Hispanic or Latino ethnicity, no. (%)	427	16 (3.7%)	9 (2.6%)	3 (7.0%)	4 (9.5%)	.04
Minority race or ethnicity ^b , no. (%)	427	87 (20.4%)	73 (21.5%)	10 (23.3%)	4 (9.5%)	.17
Education, no. (%)	427					.07
Less than GED or high school education		122 (28.6%)	103 (30.3%)	11 (25.6%)	8 (19.0%)	
Some college, no degree		154 (36.1%)	128 (37.6%)	13 (30.2%)	12 (28.6%)	
College degree or higher		151 (35.4%)	109 (32.1%)	19 (44.2%)	22 (52.4%)	
Employment status, no. (%)	427					.006
Employed		143 (33.5%)	104 (30.6%)	21 (48.8%)	17 (40.5%)	
Unemployed		88 (20.6%)	75 (22.1%)	7 (16.3%)	6 (14.3%)	
Disabled		128 (30.0%)	112 (32.9%)	9 (20.9%)	6 (14.3%)	
Out of labor force		68 (15.9%)	49 (14.4%)	6 (14.0%)	13 (31.0%)	
Income, no. (%)	427					<.001
<\$20,000/year		151 (35.4%)	133 (39.1%)	10 (23.3%)	8 (19.0%)	
\$20,000 to \$54,999/year		155 (36.3%)	128 (37.6%)	11 (25.6%)	14 (33.3%)	
\$55,000/year		121 (28.3%)	79 (23.2%)	22 (51.2%)	20 (47.6%)	
Married, no. (%)	427	127 (29.7%)	97 (28.5%)	18 (41.9%)	12 (28.6%)	.19
Sexual orientation, no. (%)	427					.58
Heterosexual or straight		382 (89.5%)	305 (89.7%)	37 (86.0%)	39 (92.9%)	
Lesbian, gay, bisexual, or other		45 (10.5%)	35 (10.3%)	6 (14.0%)	3 (7.1%)	
Rural residence, no. (%)	427	98 (23.0%)	82 (24.1%)	11 (25.6%)	4 (9.5%)	.09

Abbreviations: %, percentage; GED, General Education Development; SD, standard deviation. ^aThe 'Overall' column includes all participants randomized to the study, including n=2 participants whose recruitment source is unknown. ^b'Minority race or ethnicity' includes all participants who indicated a race other than White race and Hispanic/Latinx participants of any race.

Cancer-related characteristics of participants by recruitment strategy

Over 32 types of cancer were represented in the trial. Breast cancer was the most common

diagnosis (n=129/427, 30.2%), followed by lung cancer (n=96/427, 23.8%), and gynecologic (n=33/427, 7.7%) cancers (i.e., cervical, ovarian, vaginal, endometrial, uterine, and vulvar) (**Table 4**). Cancer patients with all stages of

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Table 4. Cancer-related characteristics of participants by recruitment strategy

Characteristic	n	Overall ^a n=427	Recruitment source			P value
			Social media n=340 (79.6%)	Internet sites n=43 (10.1%)	Clinic n=42 (9.8%)	
Cancer type diagnosis, no. (%)	427					<.001
Breast		129 (30.2%)	108 (31.8%)	12 (27.9%)	9 (21.4%)	
Lung		96 (22.5%)	81 (23.8%)	10 (23.3%)	5 (11.9%)	
Gynecologic ^b		33 (7.7%)	27 (7.9%)	3 (7.0%)	3 (7.1%)	
Colorectal		25 (5.9%)	16 (4.7%)	4 (9.3%)	4 (9.5%)	
Head and neck ^c		20 (4.7%)	20 (5.9%)	0 (0.0%)	0 (0.0%)	
Kidney		14 (3.3%)	11 (3.2%)	3 (7.0%)	0 (0.0%)	
Leukemia		13 (3.0%)	12 (3.5%)	1 (2.3%)	0 (0.0%)	
Prostate		13 (3.0%)	9 (2.6%)	1 (2.3%)	3 (7.1%)	
Non-Hodgkin Lymphoma		11 (2.6%)	10 (2.9%)	0 (0.0%)	1 (2.4%)	
Bladder		11 (2.6%)	4 (1.2%)	2 (4.7%)	5 (11.9%)	
Skin		10 (2.3%)	4 (1.2%)	3 (7.0%)	3 (7.1%)	
Thyroid		8 (1.9%)	5 (1.5%)	0 (0.0%)	2 (4.8%)	
Anal		7 (1.6%)	3 (0.9%)	3 (7.0%)	1 (2.4%)	
Pancreatic		7 (1.6%)	3 (0.9%)	3 (7.0%)	1 (2.4%)	
All others ^d		30 (7.0%)	25 (7.4%)	1 (2.3%)	4 (9.5%)	
Stage of cancer, no. (%)	427					.05
Stage 0		44 (10.3%)	34 (10.0%)	2 (4.7%)	8 (19.0%)	
Stage I		85 (19.9%)	72 (21.2%)	5 (11.6%)	7 (16.7%)	
Stage II		71 (16.6%)	56 (16.5%)	7 (16.3%)	8 (19.0%)	
Stage III		72 (16.9%)	57 (16.8%)	12 (27.9%)	3 (7.1%)	
Stage IV		69 (16.2%)	59 (17.4%)	6 (14.0%)	3 (7.1%)	
Unknown		86 (20.1%)	62 (18.2%)	11 (25.6%)	13 (31.0%)	
Months since initial diagnosis, mean (SD)	427	10.6 (18.9)	11.0 (19.4)	7.3 (11.9)	11.0 (20.9)	.47
Received any cancer treatment, no. (%)	427	315 (73.8%)	251 (73.8%)	35 (81.4%)	27 (64.3%)	.19
Type of cancer treatment received ^e , no. (%)	315					
Chemotherapy		187 (59.4%)	155 (61.8%)	21 (60.0%)	10 (37.0%)	.04
Radiation		119 (37.8%)	98 (39.0%)	12 (34.3%)	9 (33.3%)	.75
Surgery		125 (39.7%)	97 (38.6%)	14 (40.0%)	14 (51.9%)	.41
Hormone therapy		46 (14.6%)	38 (15.1%)	3 (8.6%)	5 (18.5%)	.49
Stem cell transplant		2 (0.6%)	2 (0.8%)	0 (0.0%)	0 (0.0%)	.78
Immunotherapy		52 (16.5%)	49 (19.5%)	2 (5.7%)	1 (3.7%)	.02
Targeted therapy		26 (8.3%)	18 (7.2%)	3 (8.6%)	4 (14.8%)	.37
Precision medicine		10 (3.2%)	9 (3.6%)	0 (0.0%)	1 (3.7%)	.52
Type of health insurance, no. (%)	427					.002
Private through employer or union		5 (1.2%)	3 (0.9%)	0 (0.0%)	2 (4.8%)	
Private self-paid		161 (37.7%)	141 (41.5%)	12 (27.9%)	7 (16.7%)	
Medicaid		96 (22.5%)	74 (21.8%)	7 (16.3%)	15 (35.7%)	
Medicare		12 (2.8%)	10 (2.9%)	0 (0.0%)	2 (4.8%)	
Other health insurance (i.e., military)		15 (3.5%)	14 (4.1%)	1 (2.3%)	0 (0.0%)	
No health insurance		101 (23.7%)	68 (20.0%)	19 (44.2%)	13 (31.0%)	
Unknown		37 (8.7%)	30 (8.8%)	4 (9.3%)	3 (7.1%)	
Advised to quit by their provider, no. (%)	427	391 (91.6%)	311 (91.5%)	39 (90.7%)	41 (97.6%)	.36
Mental health						
Positive screening for depression, no. (%)	427	276 (64.6%)	218 (64.1%)	30 (69.8%)	27 (64.3%)	.76
Positive screening for anxiety, no. (%)	427	138 (32.3%)	104 (30.6%)	20 (46.5%)	13 (31.0%)	.10

Abbreviations: %, percentage; SD, standard deviation. ^aThe 'Overall' column includes all participants randomized to the trial, including n=2 participants whose recruitment source is unknown. ^bGynecologic cancer types reported by participants were, from most to least common, cervical, ovarian, vaginal, endometrial, uterine, and vulvar. ^cHead and neck cancers reported by participants were, from most to least common, throat, mouth, esophageal, laryngeal, and adenoid cystic. ^dAll other cancers reported by participants were, from most to least common, stomach, other blood cancer, Hodgkin lymphoma, brain, testicular, thymus, neuroendocrine carcinoma, appendix, liver, peritoneal, sarcoma, uveal melanoma. ^eParticipants were able to select more than one type of treatment received.

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Table 5. Smoking behaviors and alcohol use of participants by recruitment strategy

Characteristic	n	Overall ^a n=427	Recruitment source			P value
			Social media n=340 (79.6%)	Internet sites n=43 (10.1%)	Clinic n=42 (9.8%)	
Smoking behavior						
No. of cigarettes smoked per day, mean (SD)	427	14.9 (8.8)	15.2 (8.8)	14.4 (9.1)	13.7 (8.7)	.56
FTCD score, no. (%)	427	5.2 (2.1)	5.3 (2.0)	4.9 (2.4)	4.4 (2.0)	.02
High nicotine dependence (FTCD 6), no. (%)	427	206 (48.2%)	176 (51.8%)	18 (41.9%)	11 (26.2%)	.005
First cigarette within 5 min of waking, no. (%)	427	171 (40.0%)	150 (44.1%)	15 (34.9%)	5 (11.9%)	<.001
Smokes more than one-half pack per day, no. (%)	427	251 (58.8%)	204 (60.0%)	23 (53.5%)	23 (54.8%)	.61
Smokes more than 1 pack per day, no. (%)	427	51 (11.9%)	40 (11.8%)	6 (14.0%)	5 (11.9%)	.91
Smoked for ≥10 years, no. (%)	427	420 (98.4%)	333 (97.9%)	43 (100.0%)	42 (100.0%)	.41
Used e-cigarettes in past month, no. (%)	427	115 (26.9%)	97 (28.5%)	10 (23.3%)	7 (16.7%)	.22
Quit attempts in past 12-months, mean (SD)	418	2.2 (4.6)	2.1 (4.5)	2.2 (2.8)	3.1 (6.5)	.40
Confidence to quit smoking ^b , mean (SD)	426	65.6 (27.6)	66.1 (27.5)	63.5 (27.7)	63.7 (26.7)	.74
Friend and partner smoking						
Close friends who smoke, mean (SD)	427	2.1 (1.7)	2.2 (1.7)	1.8 (1.6)	1.7 (1.6)	.15
No. of housemates who smoke, mean (SD)	427	1.3 (0.8)	1.3 (0.7)	1.1 (0.8)	1.2 (1.2)	.14
Living with partner who smokes, no. (%)	427	122 (28.6%)	104 (30.6%)	12 (27.9%)	5 (11.9%)	.04
Alcohol use						
No. of drinks per drinking day, mean (SD)	421	1.0 (2.2)	1.0 (2.3)	0.9 (1.3)	1.4 (2.6)	.566
Heavy drinking ^c , no. (%)	421	30 (7.1%)	24 (7.2%)	1 (2.4%)	5 (11.9%)	.239

Abbreviations: %, percentage; FTCD, Fagerström Test for Cigarette Dependence; SD, standard deviation. ^aThe 'Overall' column includes all participants randomized to the trial, including n=2 participants whose recruitment source is unknown. ^bRange, 0-100, where 0 indicates not at all confident and 100 indicates extremely confident. ^cHeavy drinking is defined as 4 or more drinks on a typical drinking day for women and 5 or more drinks on a typical drinking day for men within the past 30 days.

cancer were represented in the trial, including 16.9% and 16.2% with stage III and IV, respectively. Mean time since diagnosis was 10.6 (18.9) months. Most participants reported receiving chemotherapy (59.4%), followed by radiation (37.8%), surgery (39.7%), and immunotherapy (16.5%). More than a third (37.7%) reported having private health insurance, 23.7% were uninsured, and 22.5% had Medicaid. Most participants reported having received advice to quit smoking from their healthcare providers (91.6%). As for mental health screening, most participants (64.6%) screened positive for experiencing depression symptoms and about one third (32.3%) screened positive for anxiety.

Social media-recruited participants were more diverse with regards to cancer types (32 vs. 16 cancer types via clinics vs. 14 cancer types via Internet sites; $P=.01$) and later stages (stage IV: 17.4% vs. 14.0% Internet vs. 7.1% clinics, $P=.05$). Type of health insurance differed across recruitment strategies. Social media-recruited participants were more likely to have private self-paid health insurance (41.5% vs. 27.9% Internet vs. 16.7% clinics).

While clinic-recruited participants were more likely to have Medicaid (35.7% vs. 21.8% social media vs. 16.3% Internet), Internet-recruited participants were more likely to be uninsured (44.2% vs. 31.0% clinics vs. 20.0% social media). There was no difference in time since diagnosis, type of cancer treatment received, receiving advice to quit, and mental health outcomes across recruitment strategies.

Smoking behaviors characteristics of participants by recruitment strategy

Cancer patients in the trial smoked a mean of 14.9 cigarettes per day and nearly half (48.2%) had high cigarette dependence (Fagerström Test for Cigarette Dependence score of 6 or higher) (Table 5). Almost all (98.4%) had smoked for over 10 years and 26.7% used e-cigarettes in the past month. Confidence to quit smoking was moderate, with a mean score of 65.6 (SD, 27.6) out of 100 (higher score corresponds to more confidence). About a third (28.6%) of participants reported living with a partner who also smoked. Social media-recruited participants were more likely to have high cigarette dependence (51.8% vs. 41.9% Internet vs. 26.2% clin-

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Table 6. Recruitment strategies and methods used

Recruitment strategy	Recruitment method
<i>Social media</i>	
1. Facebook and Instagram paid advertisement	1. Tailored social media ads to guide potential participants to the registration website (Quit2Heal.org). 2. Increased variety in social media ads on Facebook and Instagram. 3. Included still images, single and carousel ads, and video ads with and without sound.
<i>Internet sites</i>	
2. American Cancer Society (ACS)	4. Featured the study prominently on Cancer.org main landing page with a link to Quit2Heal.org. 5. Released a press statement about the study with a link to Quit2Heal.org. 6. Leveraged ACS resources for social media campaigns, posting weekly on the ACS's Facebook page. 7. Distributed flyers at reception desks at ACS Hope Lodges nationwide. 8. Integrated study promotion into ACS events like the "Great American Smoke out" and "Relay for Life".
3. FredHutch.org	9. Featured the study on Fred Hutch.org with a link to Quit2Heal.org. 10. Distributed flyers at Fred Hutch lodging houses (Behnke House and Pete Gross House) and clinics. 11. Promoted trial via Fred Hutch organizational news stories.
<i>Clinics</i>	
4. Memorial Sloan Kettering Cancer Center	12. Distributed flyers, brochures, and waiting ticker-tape messages on room television screens. 13. Conducted remote recruitment efforts through calls, mailings, and emails to eligible patients identified by healthcare providers and electronic medical records. 14. Redesigned flyer advertisements for mailing to eligible patients. 15. Enhanced outreach by adding calls and email video ads.
5. Other hospital or medical institution	16. Hired Targeted Performance Partners to contact cancer centers in the ten states with the highest smoking rates, recruiting physicians to refer their patients and distribute flyers in their clinics. 17. Roswell Park in Buffalo, NY, and University of Kansas Medical Center in Kansas City, MO, mailed out over 4,000 study flyers combined to potential participants.
6. Listserv	18. Posted a description of the study, a link to Quit2Heal.org, and an offer to provide study flyers with QR codes for distribution at clinic sites to tobacco control researchers and clinicians at 52 US cancer centers.
<i>Traditional</i>	
7. Radio	19. Hired iHeartMedia for a four-week digital radio advertising campaign. 20. Dr. Bricker (study PI) appeared in a news segment on Seattle's King 5 channel to promote the study.

ics; $P=.01$) and were more likely to live with a partner who smoked compared to those recruited via the Internet or clinics (30.6% vs. 27.9% Internet vs. 11.9% clinics; $P=.04$). All other smoking and alcohol use behaviors were similar across recruitment strategies.

Discussion

Social media recruitment overwhelmingly accounted for the highest proportion of cancer patients enrolled in our behavioral intervention trial of a smoking cessation app (Quit2Heal). Social media recruited over eight times the number of enrolled cancer patients (79.6%)

compared with Internet sites (10.1%) and clinics (9.8%). Social media also generated a similar proportion of eligible participants compared to Internet sites and clinics (53.5% vs. 49.2% Internet vs. 50.2% clinics) and a higher proportion of cancer patients with greater levels of cigarette smoking dependence - patients who are greatly in need of accessible smoking cessation programs. Overall, the time since diagnosis was 10.6 (18.9) months, suggesting quitting smoking is a priority among cancer patients and relevant to their cancer treatments.

The use of social media significantly contributed to meeting and surpassing the recruitment

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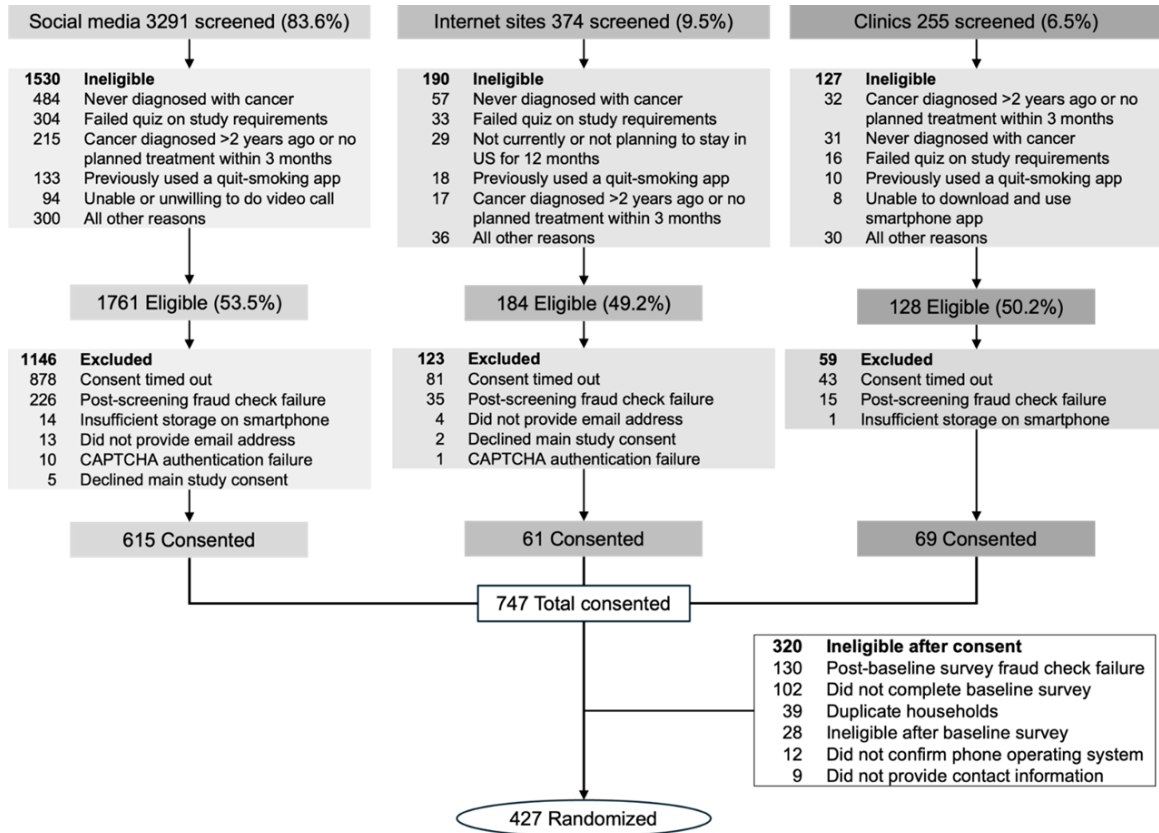


Figure 2. Recruitment and enrollment flow by recruitment strategy. Note: The percentages of screened participants do not sum 100% given that recruitment source is unknown for n=2 participants.

goal of 422 cancer patients in a timely matter. Social media generated about ten cancer patients enrolled monthly compared to one patient enrolled monthly via Internet sites, and one patient enrolled monthly via clinics. Cost per randomized participant ranged from \$270 via social media to \$454 via Internet sites to \$2,240 via clinic-based recruitment. The cost of social media recruitment in this trial was substantially lower when compared with other trials among cancer patients (\$794) [30].

In a review of studies using social media to enhance clinic-based recruitment overall, more than half (9/17; 52%) of the studies reported higher enrollment rates from social media compared to clinics, and of those, four reported that social media had the lowest cost per enrolled participant [31]. However, there were inconsistencies in social media recruitment methods and in how outcomes were reported that precluded the review's authors from making comparisons across studies. Empirical data on comparing social media to clinic-based

recruitment for cancer patients *specifically* is sparse.

Overall, the rate of participation (number of randomized/screened participants) in our study was 10.8% using a diverse recruitment approach. The other two RCTs of behavioral interventions for cancer patients that also used a mixed recruitment approach of clinic and social media have reported a wide range of participation rates (between 1.7% and 14.2%) [19, 20]. However, these rates of participation cannot be compared directly with our study given that both trials introduced social media later in the study and the period each recruitment strategy was used varied. The only known comparison is an RCT by Park et al. of behavioral telephone counseling plus medication for smoking cessation using clinic-based recruitment via electronic medical records, in which the participation rate was 6.4% (303/4709) [32]. Although a total of eight cancer types and all cancer stages were represented in that trial, the study was limited to a primarily non-

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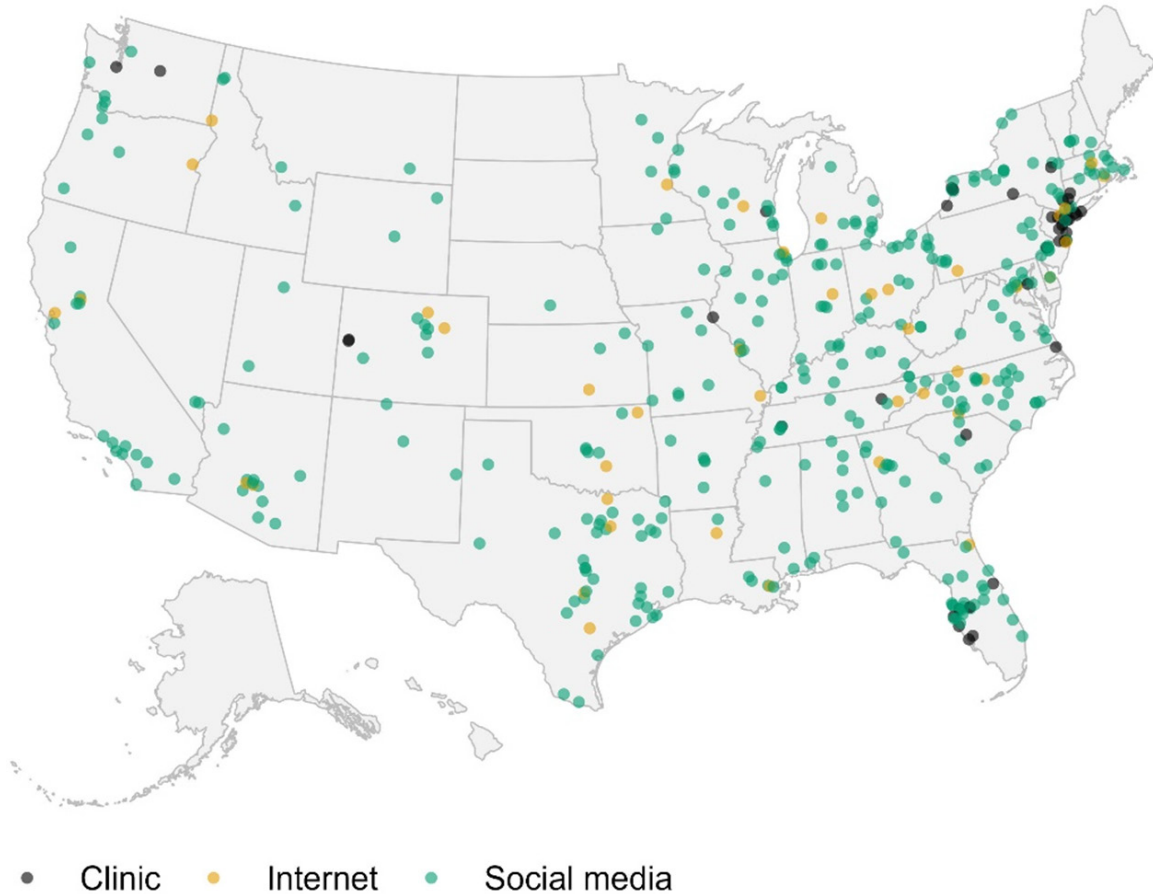


Figure 3. Geographical reach (US Map) by recruitment strategy.

Hispanic White sample (83.0%) with geographical reach to two cancer centers located in Massachusetts and New York.

In comparison, the use of social media in the current study accounted for the most diversity in terms of low socioeconomic status (39.1% low income, 30.3% low education, 22.1% unemployed), geographical reach (45 US states), and cancer types (32 types represented). These characteristics are important because people with low socioeconomic status and rare cancer types are historically underrepresented in clinical trials [33]. Compared to social media and Internet sites, clinics accounted for the highest proportion of Hispanic participants (9.5%) and patients 65 years and older (28.6%). These results suggest that clinic-based recruitment might be more efficient in enrolling cancer patients who smoke *and* are 65 years and older. Nonetheless, social media attracted a proportion of cancer patients who smoke *and* are 65 years and older that exceeded the national rate (11.5% vs. 7.2%) [34].

Overall, women (80.1%) and patients diagnosed with breast cancer (30.2%) were well-represented in our sample, with social media recruiting a significantly greater proportion of women (82.6%) compared to the Internet (69.8%) and clinics (71.4%). Well-representation of women in behavioral digital interventions is not uncommon. Both of our prior digital smoking cessation interventions, for which participants were recruited primarily via Facebook ads, also had a higher proportion of women participating (79.3% and 70.4%, respectively) [35, 36]. Indeed, social media is more likely to be used by women than men, and our results suggest the use of social media contributed to a higher proportion of women enrolled in our study [37]. While women have been historically underrepresented in cancer clinical trials, recent investigations suggest the gap is narrowing, especially for certain cancer types [33, 38]. Nonetheless, our results suggest that the use of social media could help narrow the gender gap in cancer clinical trials participation further.

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Finally, we also observed a broad representation of cancer types, cancer disease stages, and health insurance types in the trial. While social media accounted for the highest proportion of cancer patients with private health insurance, clinics accounted for the highest proportion of cancer patients with Medicaid and Medicare. Internet recruitment accounted for the highest proportion of cancer patients without health insurance, which suggests that uninsured cancer patients may be turning to the Internet for affordable cancer-related treatments, demonstrating the potential of scalable low-cost programs to reach those who are uninsured.

Our study has key limitations. First, the parent RCT was not designed to compare the effectiveness and cost of recruitment strategies [23]. Second, the trial aimed to recruit cancer patients to participate in a digital smoking cessation intervention, and thus, the findings may not be generalizable to cancer trials delivered in-person or for cancer treatment. Finally, the assessment of participants' recollection of how they found out about the study and their baseline characteristics relied on self-reports and screening tools, introducing participant subjectivity and potential reporting bias.

Considering these findings, we have two main recommendations. First, to meet recruitment goals at a lower cost and reach underrepresented cancer patients - women, racial/ethnic minorities, people with lower socioeconomic status, rural residents, and a greater representation of cancer types and stages - social media should be considered as a primary or secondary recruitment source. Clinic-based recruitment has value for reaching cancer patients 65 years and older, though the experience from this trial suggests accrual may be slower and more expensive than social media. Second, it is imperative to implement continuous monitoring of participant recruitment and make recruitment refinements (i.e., content, format, delivery) accordingly, especially among underrepresented groups in cancer clinical trials [4, 39]. For example, transitioning from the use of still images, single, and carousel ads to video ads was a key modification in our trial. This change led to a 5-fold enrollment rate increase, from approximately 4 to 20 cancer patients enrolled per month.

In conclusion, the use of social media, primarily Facebook ads, overwhelmingly surpassed Internet and clinic-based recruitment in the number of cancer patients enrolled in this trial of a digital smoking cessation intervention, especially among groups underrepresented in cancer clinical trials. Social media recruitment was also more cost-effective and allowed the trial to meet recruitment goals on time.

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Informed consent was obtained from all subjects involved in the study (Trial registration number: ClinicalTrials.gov NCT04409236).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Margarita Santiago-Torres, Cancer Prevention Program, Division of Public Health Science, Fred Hutchinson Cancer Center, 1100 Fairview Avenue North, Seattle, WA 98109, USA. Tel: 206-667-4780; Fax: 206-667-5977; E-mail: msantiag@fredhutch.org

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