JAMA Network Open

Original Investigation | Oncology

Patient Preferences for Lung Cancer Interception Therapy

Ellen M. Janssen, PhD; Ian P. Smith, MSc; Xiaoying Liu, PhD; Anna Pierce, BBA; Qing Huang, PhD; Iftekhar Kalsekar, PhD; Anil Vachani, MD, MS; Carol Mansfield, PhD

Abstract

IMPORTANCE Interception therapy requires individuals to undergo treatment to prevent a future medical event, but little is known about preferences of individuals at high risk for lung cancer and whether they would be interested in this type of treatment.

OBJECTIVE To explore preferences of individuals at high risk for lung cancer for potential interception therapies to reduce this risk.

DESIGN, SETTING, AND PARTICIPANTS This survey study used a discrete-choice experiment and included hypothetical lung cancer interception treatments with 4 attributes: reduction in lung cancer risk over 3 years, injection site reaction severity, nonfatal serious infection, and death from serious infection. Respondents were assigned to a baseline lung cancer risk of 6%, 10%, or 16% over 3 years. The discrete-choice experiment was administered online (July 13 to September 6, 2022) to US respondents eligible for lung cancer screening according to US Preventive Services Task Force guidelines. Participants included adults aged 50 to 80 years with at least a 20 pack-year smoking history. Statistical analysis was performed from September to December 2022.

MAIN OUTCOMES AND MEASURES Attribute-level preference weights were estimated, and conditional relative attribute importance, maximum acceptable risks, and minimum acceptable benefits were calculated. Characteristics of respondents who always selected no treatment were also explored.

RESULTS Of the 803 survey respondents, 495 (61.6%) were female, 138 (17.2%) were African American or Black, 55 (6.8%) were Alaska Native, American Indian, or Native American, 44 (5.5%) were Asian or Native Hawaiian or Other Pacific Islander, 104 (13.0%) were Hispanic, Latin American, or Latinx, and 462 (57.5%) were White, Middle Eastern or North African, or a race or ethnicity not listed; and mean (SD) age was 63.0 (7.5) years. Most respondents were willing to accept interception therapy and viewed reduction in lung cancer risk as the most important attribute. Respondents would accept a greater than or equal to a 12.0 percentage point increase in risk of nonfatal serious infection if lung cancer risk was reduced by at least 20.0 percentage points; and a greater than or equal to 1.2 percentage point increase in risk of fatal serious infection if lung cancer risk was reduced by at least 30.0 percentage points. Respondents would require at least a 15.4 (95% CI, 10.6-20.2) percentage point decrease in lung cancer risk to accept a 12.0 percentage point increase in risk of nonfatal serious infection; and at least a 23.1 (95% CI, 16.4-29.8) percentage point decrease in lung cancer risk to accept a 1.2 percentage point increase in risk of death from serious infection. Respondents who were unwilling to accept interception therapy in any question (129 [16.1%]) were more likely to be older and to currently smoke with no prior cessation attempt, and less likely to have been vaccinated against COVID-19 or examined for skin cancer.

(continued)

Key Points

Question Are individuals who are at high risk for lung cancer interested in potential interception therapy to reduce risk, and what are their preferences for the attributes of interception therapy?

Findings In this survey study of 803 people at high risk for lung cancer, most respondents were willing to accept interception therapy and viewed larger reductions in lung cancer risk as the most important attribute of an interception therapy.

Meaning These results suggest the importance of benefit-risk assessments for future lung cancer interception treatments.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Abstract (continued)

CONCLUSIONS AND RELEVANCE In this survey study of individuals at high risk of lung cancer, most respondents were willing to consider interception therapy. These results suggest the importance of benefit-risk assessments for future lung cancer interception treatments.

JAMA Network Open. 2023;6(11):e2342681. doi:10.1001/jamanetworkopen.2023.42681

Introduction

In the US, lung cancer is the third most common cancer diagnosed and the leading cause of cancer mortality, accounting for approximately 25% of cancer deaths.[1,2] Symptoms rarely present before lung cancer has advanced locally or spread outside the lungs; therefore, most patients are diagnosed at later stages, when prognosis is poor. Despite improvements in treatment options, lung cancer remains difficult to cure.

Cancer researchers are exploring therapies to prevent and intercept lung cancer at earlier stages, with the aim of improving outcomes and prognosis. Evidence suggests that the degree of immune cell infiltration in precancerous lung lesions may play a key role in whether the lesions progress to invasive cancers.[3] Cancer-related inflammation mediated by cytokines has also been recognized as a potential target for intervention.[4] In the Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS) trial,[5] treatment with canakinumab, an injectable monoclonal antibody targeting the interleukin-1β pathway, was associated with dose-dependent decreases in lung cancer incidence and mortality.[5] Improved understanding of immune and inflammatory drivers of cancer may facilitate the identification of markers to detect the potential for lung cancer lesions to progress and the development of systemic therapies to intercept this process.

The development of therapies to intercept potentially cancerous lung lesions poses questions that are important to address from the patient perspective. Interception therapy is associated with uncertain treatment benefit, as a person may never develop lung cancer even if not taking the interception therapy or may still develop lung cancer despite taking the interception therapy. Individuals must trade off current treatment burdens, such as potential adverse events (AEs), against uncertain future benefits. The primary objective of this study was to estimate willingness of individuals at risk of lung cancer to accept risks of up-front AEs in exchange for uncertain future treatment benefit. Additional objectives were to (1) estimate maximum level of treatment-related risk that individuals would be willing to accept in a lung cancer interception treatment in exchange for a reduction in risk of developing lung cancer for the next 3 years, (2) estimate minimum reduction in risk of lung cancer for the next 3 years that individuals would be willing to accept to compensate for treatment-related AEs, and (3) explore characteristics of individuals preferring no interception treatment.

Methods

Study Design

An online discrete-choice experiment (DCE) survey was administered (July 13 to September 6, 2022) to explore tradeoffs that participants were willing to make across treatment benefits and risks. The study followed established research practice guidelines for DCEs.[6-9] The study protocol was reviewed by the RTI International institutional review board and deemed exempt from full review. All survey respondents provided informed consent electronically. The study followed the American Association for Public Opinion Research (AAPOR) reporting guideline.[10]

Survey Development

Qualitative interviews were conducted with 23 adults at high risk of developing lung cancer to inform the selection of treatment attributes. Concerns about specific or general AEs and whether the benefit could outweigh the AEs were most frequently mentioned by interview participants.

After the interviews were conducted, a set of clinically plausible and relevant treatment attributes was developed for the survey on the basis of results from the CANTOS trial group.[5] In particular, the study team selected risk attributes related to the inflammation pathway and AEs associated with antiinflammatory agents.

The survey asked respondents to choose among 2 profiles for hypothetical interception treatments for lung cancer and an option to receive no treatment, presented in 8 DCE questions (eFigure 1 in Supplement 1). Hypothetical treatments were defined using 4 attributes with varying levels: reduction in risk of lung cancer over 3 years, severity of injection site reaction, risk of nonfatal serious infection over 3 years, and risk of death from serious infection over 3 years (eTable 1 in Supplement 1). The pairs of treatment profiles were determined by a fractional-factorial experimental design created in SAS version 9.4 (SAS Institute).[11,12]

To test the association of baseline risk of developing lung cancer and preferences, respondents were randomly assigned to 1 of 3 assumed baseline risk levels, informed by clinical expert opinion (6%, 10%, or 16% over 3 years). Three questions evaluated comprehension of the presentation of lung cancer risk reduction and nonfatal and fatal serious infection. After each comprehension question, the respondent was provided with the correct response to reinforce the material. The survey included questions to capture respondent characteristics and attitudes and evaluate understanding of the risk attribute presentation. For example, some questions asked respondents how their risks compared with "the average individual who smokes."

The survey was pretested in semistructured pretest interviews with 16 adults in the US at high risk of developing lung cancer to assess the understandability and appropriateness of the survey. Findings from the pretest interviews were used to refine the survey, particularly to ensure that presentation of the benefit attribute was clear and understandable.

Study Population

The survey was administered to US individuals at high risk of developing lung cancer, eligible for annual lung cancer screening with a low-dose computed tomography scan as recommended by the US Preventive Services Task Force.[13] Respondents were recruited by Kantar Health were eligible for the study if they were aged 50 to 80 years (inclusive); were US residents; currently smoked or had quit smoking within the past 15 years; had at least a 20 pack-year smoking history; did not have a history of lung cancer, dementia, mild cognitive impairment, or schizophrenia; and were able to read and understand English and provide informed consent (eTable 2 in Supplement 1).

Statistical Analysis

A random-parameters logit (RPL) model, or mixed logit, was developed to analyze the DCE data.[7] The RPL model has been implemented widely to analyze DCE data.[7,14] The RPL model included effect-coded variables for each attribute level and a no-treatment, alternative-specific constant (ASC), which indicated whether the no-treatment option was chosen. A positive ASC implied a preference toward treatment, whereas a negative ASC implied a preference for no treatment. A χ^2 test was used to assess whether baseline risk level for lung cancer assigned in the survey was statistically significantly associated with treatment preferences by testing the joint significance of interactions between baseline risk and the effect-coded attribute levels of reduction of lung cancer risk. Two-sided $P < .05$ was considered statistically significant.

Within an attribute, a higher preference weight estimate for a particular level indicated that that level was more preferred relative to other levels among respondents who selected an interception treatment in at least 1 DCE question. The conditional relative importance of an attribute was

calculated as the difference between the preference weights for its most-preferred and least-preferred levels; these differences were summed across attributes and scaled to 100, with the conditional importance of each attribute representing a percentage of this total. Participants' willingness to trade between treatment benefit and risks was explored by calculating the mean maximum acceptable risks participants would accept in return for a given reduction in lung cancer risk; and by calculating the mean minimum acceptable increase in reduction in the risk of lung cancer participants would accept in return for a given level of risk.

We also explored how respondent characteristics were associated with their reported willingness to choose interception treatment. A logistic model was used to explore the association between respondent characteristics (see eTable 2 in Supplement 1) and the likelihood of always choosing the no-treatment option across all 8 DCE questions. All statistical analyses were conducted using Stata/MP version 17 (StataCorp) from September to December 2022.

Results

Respondent Characteristics

In total, 838 individuals met the eligibility criteria and consented to participate. Of those, 35 (4.2%) were excluded from the analysis; 6 (17.1%) completed the survey too quickly (<6 minutes) and 29 (82.9%) did not show variability in their answers to the DCE question (always selected treatment A or always selected treatment B), leaving a total of 803 respondents included in data analysis.

Among the 803 respondents included, 495 (61.6%) were female and 308 (38.4%) were male; 138 (17.2%) self-identified as African American or Black, 55 (6.8%) as Alaska Native, American Indian, or Native American, 44 (5.5%) as Asian or Native Hawaiian or Other Pacific Islander, 104 (13.0%) as Hispanic, Latin American, or Latinx, and 462 (57.5%) as White, Middle Eastern or North African, or a race or ethnicity not listed; mean (SD) age was 63.0 (7.5) years (**Table 1**).[26] Among the 3 risk comprehension questions, question 1 was answered correctly by 618 (77.0%) respondents, question 2 was answered correctly by 553 (68.9%), and question 3 was answered correctly by 545 (67.9%); 373 (46.5%) respondents answered all questions correctly.

Preference Results

Overall, survey respondents were more likely to select systemic interception treatments than to opt out of treatment, as indicated by a positive ASC of 1.30 (95% CI, 0.91-1.69) (**Figure**; eTable 3 in Supplement 1). Respondents preferred treatments with higher relative risk reduction of lung cancer and lower risks of nonfatal serious infection or death from serious infection (Figure). No statistically significant differences in preferences were observed between severity levels of injection site reaction, indicating that respondents did not place much importance on this when making decisions considering the other attributes. Baseline risk of lung cancer (6%, 10%, or 16%) was found to not be associated with treatment preferences in a test of the joint significance of interactions between baseline risk and the effect-coded attribute levels of reduction of risk of lung cancer.

Given the included attribute levels, the change in relative risk reduction of lung cancer over 3 years from 10% to 60% had the greatest relative importance (eFigure 2 in Supplement 1). Relative risk reduction of lung cancer over 3 years (conditional relative attribute importance [cRAI]: 53.9%) was twice as important as changing the risk of death from serious infection over 3 years from 1.5% to 0.3% (cRAI: 26.9%) and approximately 3 times as important as changing the risk of nonfatal serious infection over 3 years from 15% to 3% (cRAI: 18.5%).

Maximum Acceptable Risks

Respondents would be willing to accept a greater than or equal to a 12.0 percentage point increase in risk of nonfatal serious infection over 3 years (from 3.0% to 15.0%) if the treatment could increase the relative reduction in the risk of developing lung cancer by 20.0 percentage points or more (**Table 2**). For a 10.0 percentage point increase in relative risk reduction (from 50.0% to 60.0%),

Table 1. Respondent Characteristics (N = 803)

Variable	All respondents, No. (%) (N = 803)	By DCE choice pattern, No. (%)		P value
		Chose preventive treatment at least once (n = 674)	Never chose preventive treatment (always chose opt-out) (n = 129)	
Race and ethnicity[a]				
African American or Black	138 (17.2)	121 (18.0)	17 (13.2)	.21
Alaska Native, American Indian, or Native American	55 (6.8)	47 (7.0)	8 (6.2)	
Asian or Native Hawaiian or Other Pacific Islander	44 (5.5)	40 (5.9)	4 (3.1)	
Hispanic, Latin American, or Latinx	104 (13.0)	90 (13.4)	14 (10.9)	
White, Middle Eastern or North African, or a race or ethnicity not listed	462 (57.5)	376 (55.8)	86 (66.7)	
Smoking status				
Former	311 (38.7)	254 (37.7)	57 (44.2)	<.001
Current and had ever tried quitting	357 (44.5)	319 (47.3)	38 (29.5)	
Current and had never tried quitting	135 (16.8)	101 (15.0)	34 (26.4)	
Have at least 1 other risk factor for lung cancer[b]	450 (56.0)	394 (58.5)	56 (43.4)	<.001
Age, mean (SD), y	63.0 (7.5)	62.7 (7.5)	64.5 (7.1)	.01
Gender				
Female	495 (61.6)	409 (60.7)	86 (66.7)	.20
Male	308 (38.4)	265 (39.3)	43 (33.3)	
Education				
High school or below	225 (28.0)	188 (27.9)	37 (28.7)	.95
Some college/technical school/associate's degree	376 (46.8)	315 (46.7)	61 (47.3)	
4-y College degree or higher	202 (25.2)	171 (25.4)	31 (24.0)	
Employment				
Employed/homemaker/student	292 (36.4)	253 (37.5)	39 (30.2)	.27
Retired	343 (42.7)	284 (42.1)	59 (45.7)	
Unemployed or disabled/unable to work	168 (20.9)	137 (20.3)	31 (24.0)	
Pack-years, mean (SD)	41.8 (22.7)	41.2 (23.0)	45.0 (21.0)	.08
Annual household income before tax under $30 000	294 (36.6)	242 (35.9)	52 (40.3)	.91
Have health insurance	749 (93.3)	635 (94.2)	114 (88.4)	.02
Had ever taken Lung Cancer Screening	313 (39.0)	272 (40.4)	41 (31.8)	.07
Percentage of other gender-specific screening tests one has taken, mean (SD)	59.7 (30.7)	60.8 (30.6)	54.1 (30.7)	.02
Had ever had injection site reaction before	222 (27.7)	197 (29.2)	25 (19.4)	.02
Had ever had serious infection before	248 (30.9)	219 (32.5)	29 (22.5)	.02
Subjective numeracy total score (0-15), mean (SD)[c]	13.0 (3.4)	13.1 (3.4)	12.9 (3.5)	.50
Answered all 3 comprehension questions correctly	373 (46.5)	313 (46.4)	60 (46.5)	.99
Perceived risk of getting lung cancer compared with the average individual who smokes				
Less than the average individual who smoke	176 (21.9)	137 (20.3)	39 (30.2)	<.001
Same as the average individual who smokes	432 (53.8)	377 (55.9)	55 (42.6)	
Greater than individuals who smoke	102 (12.7)	92 (13.7)	10 (7.8)	
Did not know/not sure about perceived risk of getting lung cancer compared with the average individual who smokes	93 (11.6)	68 (10.1)	25 (19.4)	
The degree that individual agreed with the statement that smoking causes lung cancer (1 = strongly disagree, 5 = strongly agree), mean (SD)[d]	4.4 (0.9)	4.5(0.8)	4.1(0.9)	<.001
The amount from a given $100 an individual was willing to invest with equal chances of it being worth 2½ times the initial investment or 0	67.4 (31.2)	68.6 (30.0)	61.5 (36.7)	.02
$0	40 (5.0)	26 (3.9)	14 (10.9)	.004
>$0 and ≤$45	104 (12.9)	85 (12.6)	19 (14.7)	
>$45 and ≤$55	211 (26.3)	179 (26.6)	32 (24.8)	
>$55 and ≤$99	232 (28.9)	206 (30.6)	26 (20.2)	
$100	216 (26.9)	178 (26.4)	38 (29.5)	

(continued)

Table 1. Respondent Characteristics (N = 803) (continued)

Variable	All respondents, No. (%) (N = 803)	By DCE choice pattern		
		No. (%)		
		Chose preventive treatment at least once (n = 674)	Never chose preventive treatment (always chose opt-out) (n = 129)	*P* value
No. of measures ever taken to avoid getting COVID-19, mean (SD)	3.3 (1.6)	3.4 (1.5)	2.8 (1.8)	<.001
Total concern scores of 3 adverse effects of the lung cancer interception treatment, mean (SD)	10.0 (2.9)	9.8 (2.9)	11.0 (2.9)	<.001

Abbreviation: DCE, discrete-choice experiment.

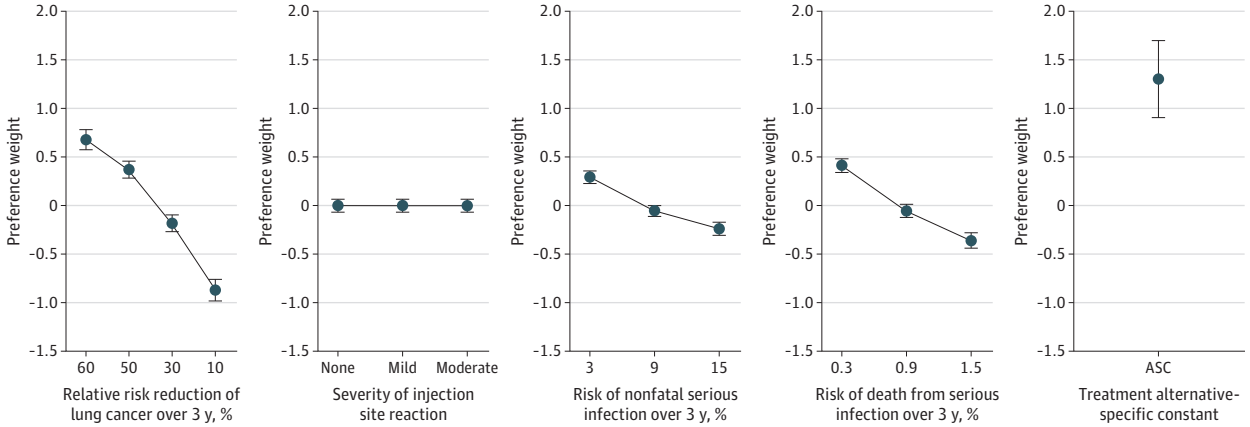
[a] Race and ethnicity were self-reported. Respondents could select all categories of race or ethnicity that applied to them. The race and ethnicity composition for those who were not White was planned on the basis of adult smoking rates among minoritized racial and ethnic populations[26] and the race distribution in population from Census data. However, some races and ethnic groups (such as Asian or Native Hawaiian or Other Pacific Islander and Hispanic, Latin American, or Latinx) were less likely to meet the inclusion criteria among individuals who smoke (in particular, the fact that they are much less likely to have a 20 pack-year smoking history). For this reason, the targeted sample sizes for Asian or Native Hawaiian or Other Pacific Islander and Hispanic, Latin American, or Latinx were not met.

[b] Risk factors included family lung cancer history, personal cancer history (other than lung cancer), and chronic obstructive pulmonary disease.

[c] The Subjective Numeracy Scale (SNS) is a self-report measure of perceived ability to perform various mathematical tasks and preferences for the use of numerical vs prose information. A higher score indicates higher self-perceived numeracy.

[d] One respondent did not provide a response to this question, and it was coded as missing for analysis purposes.

Figure. Attribute Preference Weights for Lung Cancer Interception Treatment



The preference weights reflect the tradeoffs respondents who selected an interception treatment in at least 1 discrete-choice experiment question were willing to make. A higher preference weight estimate for a particular level indicates that level was more preferred relative to other levels. The vertical bars surrounding each mean preference weight denote the 95% CI of the point estimate (preference weights computed by the delta method for the level omitted in estimation for each attribute). ASC indicates alternative-specific constant.

respondents were only willing to accept a 5.3 (95% CI, 2.6-81) percentage point increase in risk of nonfatal serious infection over 3 years (from 3.0% to 8.3%).

Respondents would accept a 1.2 percentage point increase in risk of death from serious infection over 3 years (from 0.3% to 1.5%) if the treatment could increase the relative reduction in the risk of developing lung cancer by 30.0 percentage points or more (from 10.0% to 50.0% or 60.0%, or from 30.0% to 60.0%). For smaller improvements in relative risk reduction (10.0 or 20.0 percentage point increases), respondents would accept increases in the risk of death from serious infection ranging from 0.4 to 1.0 percentage point (ie, from 0.3% to 0.7%, 1.1%, or 1.3%).

Minimum Acceptable Benefit

To accept a treatment associated with a 12.0 percentage point increase in risk of nonfatal serious infection (from 3.0% to 15.0%), respondents would require a at least a 15.4 percentage point decrease in relative risk of developing lung cancer over 3 years (Table 2). To accept a treatment associated with a 1.2 percentage point increase in risk of death from serious infection (from 0.3% to

1.5%), respondents would require at least a 23.1 percentage point decrease in relative risk of developing lung cancer (Table 2).

Respondents Who Always Selected No Treatment

Of the 803 respondents, 129 (16.1%) always selected no treatment for all choice sets, regardless of attribute levels presented. Respondents who always selected no treatment differed from other respondents in their smoking history, demographics, and opinions about preventative medicine and risk taking. Respondents who formerly smoked or currently smoked and never tried quitting, were older, had never undergone skin cancer screening nor received a COVID-19 vaccine, agreed less with the statement that smoking causes lung cancer, or had concerns about AEs of interception treatment were more likely to choose no treatment (**Table 3**). Individuals who were willing to invest less than $55 or $100 (out of $100) were more likely to choose no treatment, compared with those willing to invest between $56 and $99. Baseline risk level for lung cancer assigned to the respondent was not associated with the treatment/no treatment decision.

Discussion

When considering the potential features of lung cancer interception treatment, individuals at high risk of lung cancer were willing to accept risk of nonfatal serious infection and risk of death for most

Table 2. Maximum Acceptable Risks and Minimum Acceptable Benefit

	Change in risk reduction of lung cancer over 3 y					
	From 10.0% to 30.0% (20.0 percentage point change)	From 30.0% to 50.0% (20.0 percentage point change)	From 50.0% to 60.0% (10.0 percentage point change)	From 10.0% to 50.0% (40.0 percentage point change)	From 30.0% to 60.0% (30.0 percentage point change)	From 10.0% to 60.0% (50.0 percentage point change)
Maximum acceptable risks in exchange for a greater reduction in the risk of lung cancer						
Change in risk of nonfatal serious infection over 3 y, percentage points, mean (95% CI)[a]	≥12.0[b]	≥12.0[b]	5.3 (2.6-8.1)	≥12.0[b]	≥12.0[b]	≥12.0[b]
Change in risk of death from serious infection over 3 y, percentage points, mean (95% CI)[c]	1.0 (0.7-1.4)	0.8 (0.5-1.1)	0.4 (0.2-0.6)	≥1.2[d]	≥1.2[d]	≥1.2[d]
	Increase in risk of nonfatal serious infection over 3 y			Increase in risk of death from serious infection over 3 y		
	From 3.0% to 9.0% (6.0 percentage point change)	From 9.0% to 15.0% (6.0 percentage point change)	From 3.0% to 15.0% (12.0 percentage point change)	From 0.3% to 0.9% (0.6 percentage point change)	From 0.9% to 1.5% (0.6 percentage point change)	From 0.3% to 1.5% (1.2 percentage point change)
Minimum acceptable benefit as an increase in reduction in risk of lung cancer over 3 y for given changes in treatment-related risks						
Change in risk reduction of lung cancer over 3 y, percentage points, mean (95% CI)[e]	10.1 (6.3-13.9)	5.3 (2.0-8.7)	15.4 (10.6-20.2)	13.6 (9.4-17.8)	8.9 (5.0-12.7)	23.1 (16.4-29.8)

[a] The maximum acceptable risk of nonfatal serious infection for a given change in the benefit of treatment is shown, displayed as an increase in relative risk reduction of lung cancer over 3 years on top of risk 3%. The maximum acceptable risk was calculated based on the preference weights for the 3 levels of risk presented in the survey: 3%, 9%, and 15%. Maximum acceptable risk estimates outside the range of levels included in the study are noted as greater than 12%. It is possible to estimate a specific value for the maximum acceptable risk outside the range of levels included in the study only by making the strong assumption that the disutility of each unit increase in risk remains constant beyond the greatest level of risk (15%).

[b] Given that coefficients of effect-coded risk of nonfatal serious infection satisfy linearity, and by making the assumption in footnote a, the maximum acceptable risks (from the left to the right) are 20.16 (95% CI, 12.30-28.02), 15.70 (95% CI, 9.88-21.51), 38.20 (95% CI, 21.17-55.24), 25.80 (95% CI, 15.32-36.28), and 48.31 (95% CI, 25.15-71.46), respectively.

[c] The maximum acceptable risk of death from serious infection over 3 years for a given change in the benefit of treatment is shown, displayed as an increase in relative risk reduction of lung cancer over 3 years on top of 0.3%. Maximum acceptable risk was calculated based on the preference weights for the 3 levels of risk presented in the survey: 0.3%, 0.9%, and 1.5%. Maximum acceptable risk estimates outside the range of levels included in the study are noted as greater than 1.2%. It is possible to estimate a specific value for the maximum acceptable risk outside the range of levels included in the study only by making the strong assumption that the disutility of each unit increase in risk remains constant beyond the greatest level of risk (1.5%).

[d] Given that coefficients of effect-coded risk of death from serious infection satisfy linearity, and by making the assumption in footnote c, the maximum acceptable risks (from the left to the right) are 2.42 (95% CI, 1.83-3.01), 1.67 (95% CI, 1.29-2.06), and 3.03 (95% CI, 2.22-3.83), respectively.

[e] Minimum acceptable change in benefit as an increase in relative risk reduction of lung cancer, starting from reference level 10%, for given changes in treatment-related risks. The coefficients on any levels of injection site reaction were not statistically significant, and therefore, (1) the change from 1 level to the other of the injection site reaction attribute was not associated with respondents' preferences and (2) minimum acceptable benefit for a given change in this risk was not calculated.

Table 3. Odds Ratios of Factors Associated With Always Selecting No Treatment[a]

Factor	Specification 1		Specification 2		Specification 3		Specification 4	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Stratification variables								
White[b]	1.54 (1.02-2.31)	.04	1.42 (0.92-2.18)	.11	1.56 (1.00-2.43)	.05	1.59 (0.99-2.55)	.05
Formerly smoked[c]	0.71 (0.43-1.16)	.17	0.64 (0.38-1.08)	.10	0.64 (0.38-1.10)	.11	0.69 (0.38-1.27)	.23
Currently smokes and had ever tried quitting[c]	0.39 (0.23-0.65)	<.001	0.36 (0.21-0.62)	<.001	0.36 (0.21-0.63)	<.001	0.38 (0.21-0.70)	.002
Have at least 1 other risk factor for lung cancer	0.57 (0.38-0.84)	.005	0.55 (0.36-0.82)	.004	0.63 (0.42-0.97)	.04	0.74 (0.47-1.17)	.20
10% Baseline risk of lung cancer[d]	1.11 (0.70-1.76)	.66	1.16 (0.72-1.86)	.54	1.16 (0.72-1.87)	.53	1.12 (0.67-1.86)	.68
16% Baseline risk of lung cancer[d]	0.89 (0.55-1.43)	.62	0.95 (0.58-1.56)	.83	0.95 (0.58-1.58)	.85	0.98 (0.58-1.68)	.95
Demographic and socioeconomic characteristics								
Age	NA	NA	1.04 (1.01-1.08)	.02	1.05 (1.01-1.09)	.009	1.06 (1.02-1.10)	.007
Male	NA	NA	0.74 (0.48-1.14)	.17	0.64 (0.40-1.01)	.05	0.67 (0.41-1.09)	.10
Pack-years	NA	NA	1.00 (1.00-1.01)	.34	1.01 (1.00-1.01)	.23	1.00 (1.00-1.01)	.35
4-y College degree or above[e]	NA	NA	1.01 (0.61-1.67)	.97	1.06 (0.63-1.78)	.82	0.91 (0.52-1.59)	.73
High school education or below[e]	NA	NA	0.87 (0.54-1.41)	.57	0.81 (0.50-1.32)	.40	0.69 (0.41-1.17)	.17
Retired[f]	NA	NA	0.94 (0.54-1.64)	.83	0.96 (0.55-1.68)	.89	0.78 (0.43-1.42)	.42
Unemployed or disabled/unable to work[f]	NA	NA	1.68 (0.94-3.00)	.08	1.69 (0.93-3.05)	.08	1.84 (0.98-3.44)	.06
Annual household income before tax is less than $30 000	NA	NA	1.18 (0.76-1.83)	.45	1.11 (0.71-1.73)	.65	1.06 (0.67-1.69)	.81
Have health insurance	NA	NA	0.40 (0.20-0.79)	.009	0.47 (0.23-0.93)	.03	0.53 (0.25-1.14)	.10
Other health behavior								
Had lung cancer screening before	NA	NA	NA	NA	0.82 (0.52-1.27)	.37	0.92 (0.57-1.48)	.74
Had ever received an examination to check for skin cancer or precancerous moles[g]	NA	NA	NA	NA	0.49 (0.29-0.81)	.006	0.56 (0.33-0.95)	.03
Had injection site reaction before	NA	NA	NA	NA	0.64 (0.38-1.07)	.09	0.69 (0.40-1.19)	.18
Had serious infection before	NA	NA	NA	NA	0.76 (0.47-1.24)	.28	0.60 (0.35-1.01)	.06
Numeracy and comprehension								
Total subjective numeracy score	NA	NA	NA	NA	1.01 (0.95-1.08)	.74	1.03 (0.96-1.10)	.43
Answer all 3 comprehension questions correctly	NA	NA	NA	NA	1.04 (0.69-1.55)	.87	1.17 (0.76-1.80)	.49
Risk preference and attitude								
Perceived risk of lung cancer is lower than the average person who smokes[h]	NA	NA	NA	NA	NA	NA	1.57 (0.91-2.70)	.11
Perceived risk of getting lung cancer is higher than the average person who smokes[h]	NA	NA	NA	NA	NA	NA	1.05 (0.48-2.32)	.90
Do not know/not sure about perceived risk of getting lung cancer compared to the average person who smokes[h]	NA	NA	NA	NA	NA	NA	1.78 (0.96-3.31)	.07
Degree of agreement with the statement that smoking causes lung cancer (1 = strongly disagree, 5 = strongly agree)	NA	NA	NA	NA	NA	NA	0.70 (0.54-0.89)	.004
Willing to invest $0-$45 from a given $100 with equal chances of it being worth 2½ times the initial investment or zero[i]	NA	NA	NA	NA	NA	NA	0.58 (0.22-1.51)	.26
Willing to invest $46-$55 from a given $100 with equal chances of it being worth 2½ times the initial investment or zero[i]	NA	NA	NA	NA	NA	NA	0.49 (0.20-1.19)	.12
Willing to invest $56-$99 from a given $100 with equal chances of it being worth 2½ times the initial investment or zero[i]	NA	NA	NA	NA	NA	NA	0.34 (0.13-0.83)	.02
Willing to invest $100 from a given $100 with equal chances of it being worth 2½ times the initial investment or zero[i]	NA	NA	NA	NA	NA	NA	0.61 (0.25-1.48)	.27
Had received a COVID-19 vaccine[j]	NA	NA	NA	NA	NA	NA	0.54 (0.33-0.87)	.01
Total score of concern for 3 adverse effects of the lung cancer interception treatment	NA	NA	NA	NA	NA	NA	1.22 (1.12-1.32)	<.001
Constant	0.33 (0.19-0.56)	<.001	0.04 (0.01-0.39)	.005	0.03 (0.00-0.31)	.003	0.02 (0.00-0.38)	.009

(continued)

Table 3. Odds Ratios of Factors Associated With Always Selecting No Treatment[a] (continued)

Factor	Specification 1		Specification 2		Specification 3		Specification 4	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Respondents, No.	803	NA	803	NA	803	NA	802	NA
χ^2 test	30.98	NA	49.83	NA	65.86	NA	128.5	NA
P value for model test	<.001	NA	<.001	NA	1.59e-06	NA	0	NA
Log-likelihood	−338.4	NA	−329.0	NA	−321.0	NA	−289.5	NA

Abbreviations: NA, not applicable; OR, odds ratio.

[a] Table 3 includes the results from a logit regression of binary choice of always choosing no treatment vs sometimes or never choosing no treatment on a series of regressors together. The results from 4 different specifications of the logit model are presented, with the dependent variable defined as 1 if the individual always selected no treatment throughout all the discrete-choice experiment questions, and 0 otherwise. Specification 1 included the prespecified stratification variables. Specification 2 added a list of basic demographic and socioeconomic variables in addition to the variables included in specification 1. Specification 3 added a list of variables that measure other health-related behavior, numeracy, and comprehension in addition to the variables included in specification 2. Specification 4 added respondents' risk preference and attitude, as well as total scores of the concern over 3 adverse effects of the treatment in addition to the variables included in specification 3. ORs higher than 1 indicate higher likelihood to select no treatment over treatment.

[b] Regressions with each race and ethnicity group as a separate dummy variable (with White as a reference group) were also tried, with no significant difference across race and ethnicity groups in terms of decision to have no treatment. Race and ethnicity groups other than White were therefore combined into 1 group and compared with the White group.

[c] Reference group is people who currently smoke and have never tried quitting smoking.

[d] Reference group is those who were assigned to baseline level of lung cancer risk at 6%.

[e] Reference group is those who have some college but no degree, or technical school education or associate degree.

[f] Reference group is those who are employed (full- or part-time) or self-employed, homemaker, or student.

[g] Other screening tests (eg, colonoscopy or other colon screening test) and preventive health measures (eg, influenza shot or medicine to reduce risk of heart problems, high blood pressure, or high cholesterol) were tried individually or jointly with the variable: "Had received an examination to check for skin cancer or precancerous moles." Only "Had received an examination to check for skin cancer or precancerous moles" was significant consistently across the models.

[h] Reference group is those who believe their self-risk of getting lung cancer without treatment is the same as the average person who smokes in the US.

[i] Reference group is those who were willing to invest $0 out of the given $100 for an investment opportunity with equal chances of it being worth 2½ times the initial investment or 0.

[j] Other precautionary measures an individual has taken to protect their family and themselves from getting COVID-19 (eg, wearing masks indoors when outside the home, washing hands as often as possible) were also tried individually or jointly with "had received a COVID vaccine." Only "Had received a COVID vaccine" remained consistently significant.

reductions in the risk of developing lung cancer. Respondents generally preferred treatment over no treatment, with 16.1% of respondents selecting no treatment in all DCE scenarios. The randomly assigned baseline risk of lung cancer presented in the survey was not associated with preference for treatment; participants who were assigned a 6% risk of lung cancer in the next 3 years were not more or less likely to opt out of treatment than participants who were assigned a risk of 10% or 16%.

To our knowledge, this study is the first to investigate preferences for interception treatment to reduce lung cancer risk. However, previous DCE surveys have examined preferences for preventive treatments. Liede et al[15] found that women with *BRCA1* or *BRCA2* variants were willing to accept risk of developing secondary uterine cancer to reduce their chance of developing breast cancer. Simons et al[16] found that respondents were generally willing to tolerate some risk of serious AEs (eg, brain inflammation, lymphoma, or retinopathy) to reduce the risk of developing rheumatoid arthritis, although this willingness diminished as treatment efficacy was reduced and the risks increased. Minnis et al[17] found that both efficacy and product characteristics affected choice of human immunodeficiency virus prevention products among young women in Kenya and South Africa. In a study of mothers' preferences for a rotavirus vaccine, Poulos et al[18] found that the relative importance of the effectiveness of the vaccine varied by country and by mothers' employment status. The results of these studies are consistent with our findings that effectiveness is a primary driver of individuals' preferences for preventive therapy, although this may vary based on disease, treatment, and personal characteristics.

A relatively large proportion of participants (16.1%) were unwilling to accept preventive therapy at all. Preferences were also associated with avoidance of other preventive measures (eg, cancer screening), suggesting that some individuals may not prefer preventive care in general. Respondents more likely to choose the no-treatment option also agreed less with the statement that smoking causes lung cancer and were less sure of their personal risk compared with an average person who smokes. Similar to our findings, Simons et al[16] found that approximately 14% of respondents would

likely choose no treatment when presented with a hypothetical preventive rheumatoid arthritis treatment and that preferences for no treatment were associated with lower perceived chance of developing the disease. Future qualitative research should explore the reasoning behind opting out of preventive care to better understand these preferences.

The baseline risk of lung cancer assigned randomly in the survey was not associated with preference for treatment or likelihood of opting out of preventive therapy. Previous studies that have explored treatment preferences by estimating willingness to pay (as opposed to willingness to accept risk, as in our study) have been inconclusive regarding the effect of the baseline risk on preferences.[19-23] Future research could explore further how baseline risk influences decision-making, particularly in the context of preventive therapy.

Our study has several strengths derived from the use of best practices in its design and analyses.[6-8,24] Qualitative interviews were conducted to identify the features of interception treatments relevant to individuals considering preventive treatment. The final survey was carefully designed and pretested during in-depth interviews to confirm comprehensibility. The use of 3 different baseline risk levels allowed us to evaluate the chance of bias if a respondent did not see the initial risk as sufficiently high to warrant treatment. A key strength of the study was its size, with more than 800 respondents allowing for analyses to identify subgroups of respondents with unique preferences.

Limitations

This study had limitations. The DCE choice questions were complex. Although 68% to 77% of respondents answered each individual comprehension question correctly, similar to what was observed in other studies,[25] half the respondents failed to answer all comprehension questions correctly. We controlled for incorrect responses to all 3 comprehension questions in the analyses and did not find this indicator to have significant correlation with the binary outcome of choosing treatment over no treatment. Furthermore, the baseline risk of developing lung cancer presented in the survey was not significantly associated with respondents' treatment preferences or their likelihood of choosing no treatment, but it is possible that the range of baseline risks presented (6% to 16%) was too small to influence treatment preferences. The sample was recruited through an online research panel, which may not reflect the US population who meet the eligibility criteria for the study. The extent to which the sample is underrepresentative of those who are unwilling to accept interception therapy is uncertain. Data collected in DCEs are based on responses to hypothetical choice profiles, which are intended to simulate possible clinical decisions but do not have the consequences of actual clinical decisions. Additionally, the study aimed to recruit a sample with sufficient diversity in race and ethnicity to estimate those factors' associations with preferences; however, targeted sample sizes for individuals of certain races and ethnicities (eg, Asian or Native Hawaiian or Other Pacific Islander; Hispanic, Latin American, or Latinx) were not met. These groups were found to be more likely to be screened out of the survey because they were less likely than other groups to have a smoking history of at least a 20 pack-years.

Conclusions

In this survey study, individuals at high risk of developing lung cancer generally preferred higher relative risk reduction with lower risk of AEs. Most individuals were willing to trade off benefit and risks of interception treatment, but the extent of the tradeoffs varied systematically. These results suggest the importance of benefit-risk assessments for future systemic lung cancer interception treatments and may have implications for other therapeutic areas.

ARTICLE INFORMATION

Accepted for Publication: October 2, 2023.

Published: November 10, 2023. doi:10.1001/jamanetworkopen.2023.42681

Corresponding Author: Ellen M. Janssen, PhD, Global Epidemiology, Janssen Research and Development, 1125 Trenton Harbourton Rd, Titusville, NJ 08560 (ejansse5@its.jnj.com).

Author Affiliations: Global Epidemiology, Janssen Research and Development, Titusville, New Jersey (Janssen, Smith); Interventional Oncology, Johnson & Johnson External Innovation, New Brunswick, New Jersey (Smith, Huang, Kalsekar); RTI Health Solutions, Research Triangle Park, North Carolina (Liu, Pierce, Mansfield); University of Pennsylvania Perelman School of Medicine, Philadelphia (Vachani).

Author Contributions: Dr Liu and Dr Mansfield had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Janssen, Liu, Pierce, Huang, Kalsekar, Mansfield.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Janssen, Smith, Liu.

Critical review of the manuscript for important intellectual content: All authors.

Statistical analysis: Smith, Liu, Pierce, Mansfield.

Obtained funding: Kalsekar.

Administrative, technical, or material support: Janssen, Smith, Liu, Pierce, Huang, Kalsekar.

Supervision: Janssen, Smith, Huang, Kalsekar, Vachani, Mansfield.

Conflict of Interest Disclosures: Dr Janssen reported being a Johnson & Johnson employee during the conduct of the study; and being a Johnson & Johnson stockholder and employee outside the submitted work. Dr Smith reported personal fees from Janssen Pharmaceutical outside the submitted work. Dr Liu reported being a full-time employee of RTI Health Solutions and compensation was unconnected to the projects on which Dr Liu worked during the conduct of the study. Dr Pierce reported being a full-time employee of RTI Health Solutions and compensation was unconnected to the projects on which Dr Pierce worked during the conduct of the study. Dr Huang reported receiving salary and stocks from Johnson & Johnson outside the submitted work. Dr Kalsekar reported being a Johnson & Johnson employee during the conduct of the study. Dr Vachani reported personal fees from Johnson & Johnson during the conduct of the study; and grants from Precyte Inc, grants from Optellum Ltd, grants from Median Technologies, personal fees from Intuitive Surgical, and grants from National Comprehensive Cancer Network/Astra Zeneca outside the submitted work. Dr Mansfield reported being a full-time employee of RTI Health Solutions and compensation was unconnected to the projects on which Dr Mansfield worked during the conduct of the study. No other disclosures were reported.

Funding/Support: This study was conducted under a research contract between Lung Cancer Initiative, Johnson & Johnson External Innovation, and RTI Health Solutions; and was funded by Lung Cancer Initiative, Johnson & Johnson External Innovation.

Role of the Funder/Sponsor: Authors affiliated with Johnson & Johnson External Innovation and with Janssen Research and Development participated in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See Supplement 2.

Additional Contributions: Kimberly Moon, BA, BS, PMP, RTI Health Solutions, provided overall project management for this study. Ms Moon was not compensated outside of regular salary for her contributions. Kate Lothman, BA, RTI Health Solutions, provided medical writing services, which were funded by Janssen.

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SUPPLEMENT 1.

eTable 1. Attributes and Levels for the Discrete-Choice Experiment Survey
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SUPPLEMENT 2.

Data Sharing Statement