A randomized survey study of structured reflective questions and willingness to participate in window of opportunity trials

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BACKGROUND

•Window of Opportunity Trials allow biological assessment of investigational drugs in the interval between cancer diagnosis and planned treatment. These trials rarely offer direct benefit but require additional procedures and may delay treatment.

•Qualitative interviews in breast cancer survivors found high willingness to participate, tempered by concerns about safety, logistics, and potential delays.

•Understanding how brief, structured reflective questions may influence patient willingness can inform low-burden strategies to improve patient-centered trial engagement.

AIMS

•Determine the effect of brief, structured reflective questions on breast cancer survivors' willingness to participate in a WOT.

•Assess demographic, clinical, and attitudinal predictors including research distrust are associated with willingness to participate.

METHODS

•Eligible participants included adults with a history of stage 0–III breast cancer (N=874) who completed an online survey between March 2022 and May 2025.

•Participants first viewed a visual explanation of a Window-of-Opportunity Trial (WOT), illustrating investigational treatment between diagnosis and planned standard therapy, including potential added biopsies and possible delays.

•Participants were randomized (2:1) to either:
- •**Reflective Question Arm**: answered neutral questions on barriers (biopsies, delays, clinic visits) and motivators (altruism, scientific contribution) *before* being asked about willingness.
- •**Control Arm**: asked about willingness immediately.

•The primary endpoint was willingness to participate (Likert scale). Secondary variables included demographics, cancer history, prior research participation, and the Corbie-Smith Research Distrust Index.

Figure 1: Consort Diagram

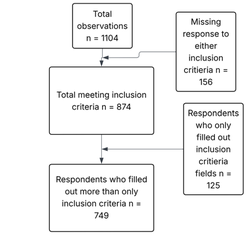


Figure 2: Visual Representation of WOT



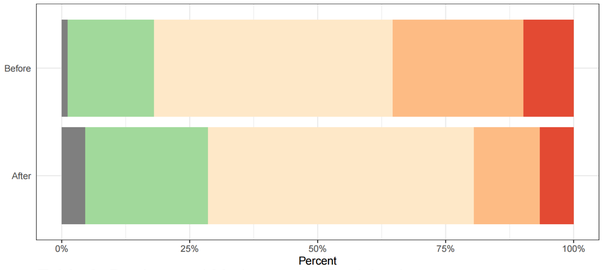
RESULTS

Table 1: Association of Participant Characteristics with Agreement to Participate

[a]Characteristic	Disagree to Participate	Agree to Participate	p-value
Exposure to reflective Questions			<0.001
Before	94 (50%)	169 (32%)	
After	94 (50%)	367 (68%)	
Age			0.125
18-30 years	1 (0.5%)	7 (1.3%)	
31-50 years	73 (40%)	232 (44%)	
51-65 years	75 (41%)	222 (42%)	
65+ years	33 (18%)	72 (14%)	
No response	6	3	
Race and Ethnicity			0.4
White, non-Hispanic	150 (81%)	428 (82%)	
Black	9 (4.8%)	19 (3.7%)	
Hispanic	9 (4.8%)	19 (3.7%)	
Asian	11 (5.9%)	40 (7.7%)	
Native American / Alaska Native,	0 (0%)	2 (0.4%)	
Native Hawaiian or Other Pacific Islander	0 (0%)	2 (0.4%)	
Other	3 (1.6%)	7 (1.3%)	
Prefer not to say	4 (2.2%)	2 (0.4%)	
No response	2	17	
Gender			>0.9
Female	185 (100%)	513 (99.6%)	
Male	0 (0%)	1 (0.2%)	
Non-binary / third gender	0 (0%)	1 (0.2%)	
I prefer not to say	0 (0%)	0 (0%)	
No response	3	21	
Education			0.0794
High school diploma or less	14 (7.6%)	58 (11%)	
Associate's degree or technical certification	22 (12%)	87 (17%)	
Bachelor's degree	68 (37%)	174 (34%)	
Master's degree	62 (34%)	139 (27%)	
Professional or doctorate degree	19 (10%)	58 (11%)	
No response	3	20	
Income			0.124
Less than $25,000	3 (1.7%)	17 (3.4%)	
$25,000 - $49,000	12 (6.8%)	39 (7.7%)	
$50,000 - $75,000	17 (9.7%)	66 (13%)	
$75,000 - $100,000	39 (22%)	91 (18%)	
$100,000 - $150,000	30 (17%)	113 (22%)	
More than $150,000	75 (43%)	179 (35%)	
No response	12	31	
Insurance			0.3
Private health insurance	142 (76%)	405 (78%)	

[a] "Disagree" includes responses of Strongly Disagree and Somewhat Disagree; "Agree" includes responses of Somewhat Agree and Strongly Agree.
[b]includes: Medicare, Medicaid, Military, State-sponsored plan, or other governmental program

Figure 3: Patient willingness to participate in a window of opportunity clinical trial



- Participants asked *after* the contextual questions are significantly ($p < 0.001$) more likely to report a greater willingness to participate, compared to those asked *before*.

Table 2: Barriers and Motivators for Participation

Characteristic	N = 749[1]
How many additional biopsies would you be willing to have as part of a "window of opportunity" clinical trial?	
0 biopsies	125 (17%)
1 biopsy	325 (44%)
2 biopsies	151 (20%)
3 or more biopsies	142 (19%)
No response	6
If participation in a "window of opportunity trial" increased the time to start of treatment, how many additional weeks would be acceptable to you to wait?	3 (3)
No response	67
How many additional clinic visits would you be willing to have?	
0 visits	35 (4.7%)
1 visit	51 (6.8%)
2 visits	133 (18%)
3 visits	120 (16%)
4 visits	104 (14%)
5 or more visits	304 (41%)
No response	2
Which of the following factors would negatively influence your decision to participate in a "window of opportunity" clinical trial (select all that apply):	
The need for more biopsies to be used for research purposes only	35 (6.9%)
The time it would take for additional clinic visits or laboratory testing for the purposes of research only	20 (3.9%)
Potential delay in my surgery or other planned treatment	368 (72%)
None of the above	87 (17%)
No response	239

[1] n (%); Mean (SD)

Table 3: Clinical Distrust and Participation

Characteristic	Disagree to Participate N = 188[1]	Agree to Participate N = 536[1]	P-value[2]
If your doctor wanted you to participate in research, you trust that he/she would fully explain it to you. (Disagree/I don't know)	42 (23%)	52 (10%)	<0.001
Do you believe that you can freely ask your doctors any questions that you want? (No/I don't know)	16 (8.7%)	37 (7.2%)	0.5
Your doctor would not ask you to participate in medical research if he/she thought it would harm you. (Disagree/I don't know)	49 (27%)	76 (15%)	<0.001
Do you believe that doctors have ever given you treatment as part of an experiment without your permission? (Yes/I don't know)	16 (8.8%)	29 (5.7%)	0.14
How likely is it that you, or people like you, might be used as guinea pigs in research studies without your consent? (Very likely/Somewhat likely/I don't know)	56 (30%)	101 (20%)	0.003
How often, if ever, do you think doctors prescribe medication as a way of experimenting on people without their knowledge or consent? (Very often/Fairly often/I don't know)	47 (25%)	100 (20%)	0.10
In deciding what treatments you will get, do you feel that your doctors always try to protect you from unnecessary risk, or do you feel that they sometimes expose you to unnecessary risk? (Sometimes expose to unnecessary risk/I don't know)	90 (50%)	215 (42%)	0.078

[1] n (%); [2] Pearson's Chi-squared test

CONCLUSIONS

- After answering reflective questions about barriers and motivators, participants showed significantly greater willingness to participate in a window-of-opportunity trial
- The impact of reflective-question exposure on willingness was much larger than the influence of demographic or clinical factors.
- This highlights the potential for scalable behavioral strategies to enhance patient engagement in clinical trials.

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