

Assessment of Health State Utilities Associated with False-Positive Cancer Screening Results

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BACKGROUND AND OBJECTIVE

- Early cancer detection and intervention can significantly improve patient outcomes and reduce mortality rates.¹ A simple procedure that can detect multiple types of cancer could significantly improve patient outcomes. One such possible procedure uses plasma cell-free DNA (cfDNA) to identify cancer via a simple blood draw.²
- An effective cfDNA-based cancer screening test would ideally detect a variety of cancers across stages, predict cancer signal origin, and have very high specificity (i.e., a very low rate of false positive [FP] results³).
- When evaluating multi-cancer early detection (MCED) tests, it will be important to consider the incidence rate and impact of FP results, which can have a psychological impact on patients. To incorporate the impact of FP results into cost-effectiveness models to determine the value of novel cancer screening approaches, health state utilities representing FPs are needed.
- A vignette-based utility elicitation study was conducted in November 2021 to estimate the disutility associated with FPs in four types of cancer with various follow-up testing pathways.

METHODS

Study Design

- Vignette-based time trade-off (TTO) utility interviews were conducted with a sample of general population respondents in London, United Kingdom.
- Ten health states were drafted (see examples of health states in Figure 1). Health state A (true negative) stated that participants had undergone routine cancer screening with negative results. All other health states described an FP experience as follows.
 - A statement indicating that the participant had undergone routine screening, received a positive result for a specific type of cancer, and required follow-up diagnostic testing (specific for each cancer type).
 - Descriptions of additional diagnostic follow-up procedures, including computed tomography (CT) scan, magnetic resonance imaging (MRI), positron emission tomography/computed tomography (PET-CT), mammogram, breast ultrasound, and/or colonoscopy, depending on the type of cancer indicated by the test result. Images were provided to show participants the type of machinery for each test.
 - Statements indicating the diagnostic follow-up tests revealed that the screening result was an FP.
 - The total amount of time from initial screening to final confirmation of the FP result was provided, along with a timeline illustrating the sequence of testing events and results.



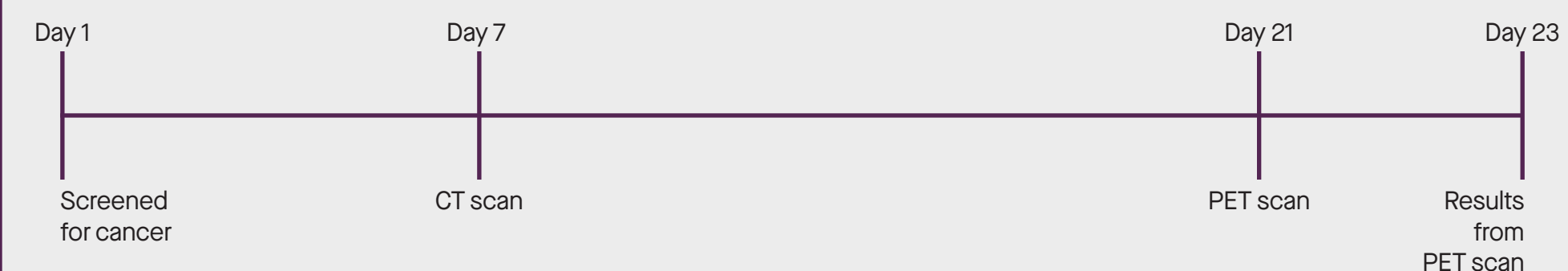
Participants

- All participants were required to be (1) at least 18 years of age; (2) able to understand the assessment procedures as judged by the investigator; (3) able and willing to give written informed consent; (4) able to complete the protocol requirements; and (5) a UK resident.

Health State Development

- Health states were drafted based on: (1) published literature on cancer screening procedures; and (2) interviews with five clinicians, including two oncologists, one pulmonologist, one radiologist, and one anesthesiologist, all with experience in cancer screening procedures. Interviews were also conducted with one academic professor who works with the UK National Screening Committee to advise the UK government on appropriate cancer screening procedures and recommendations for the UK population.
- Health states were drafted in an iterative process, with multiple rounds of expert interviews. Health states and procedures were also tested in a pilot study with 30 participants (mean [SD] age 45.8 [14.5] years; 50.0% male). Minor edits to health state formatting and word choice were made based on pilot participant feedback.

Figure 1. Sample Health State E2: Pancreatic with PET-CT

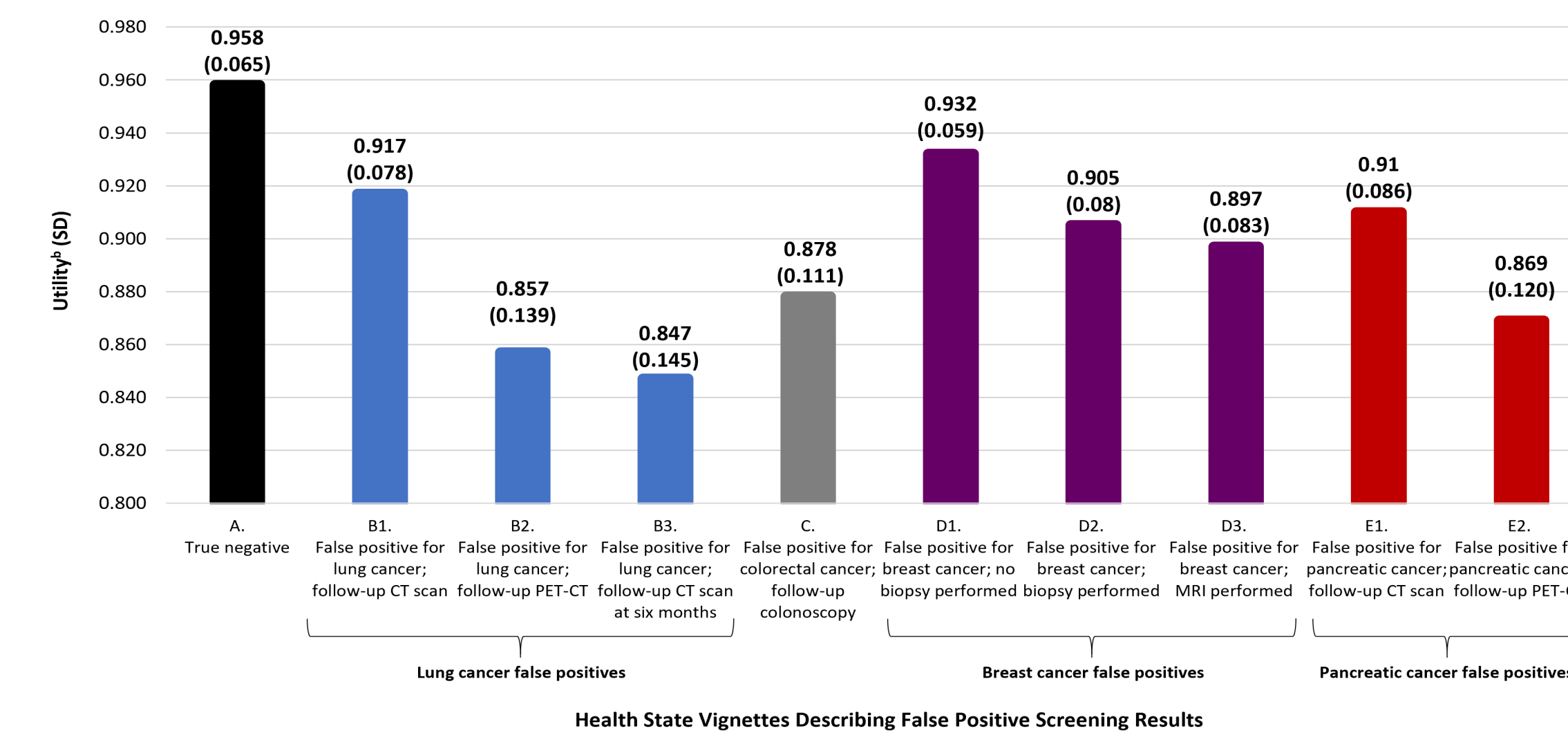
Cancer Screening	As part of a routine health check, you are screened for cancer.
Screening Result	<ul style="list-style-type: none"> The screening results suggest you may have pancreatic cancer. Therefore, more testing is needed.
CT Scan	<ul style="list-style-type: none"> You attend an appointment for a scan of your abdomen (called a CT scan). This scan will create an image of your pancreas. One hour before the procedure, you drink a bad-tasting liquid. This will help create a more detailed image of your pancreas. <ul style="list-style-type: none"> This liquid causes some diarrhea and cramping. The full procedure takes about 60 minutes. The scan itself takes a few minutes. During this time, you lie on your back in a large, ring-shaped machine. <ul style="list-style-type: none"> In preparation for this scan, you receive an intravenous (IV) injection of dye (called contrast) which helps create a more detailed image of your pancreas. <ul style="list-style-type: none"> This means that a needle is inserted into a vein in your arm, and fluid flows into your body. During the injection of the dye, you may feel flushed or lightheaded. This appointment requires you to take a few hours off work. This scan takes place about one week after receiving your initial screening results. 
PET-CT Scan	<ul style="list-style-type: none"> As a final precaution, you attend an appointment for a scan of your full body (called a PET-CT scan). This scan will create a detailed image of your entire body. This scan occurs about two weeks after the CT scan. You may not eat any sugar for 24 hours before the scan. The full procedure takes about four hours. <ul style="list-style-type: none"> Prior to the scan, you receive an intravenous (IV) injection of radioactive sugar which helps create a more detailed image of your pancreas. <ul style="list-style-type: none"> This means that a needle is inserted into a vein in your arm, and fluid flows into your body. Then you wait 60-90 minutes. When it is time for the scan, you lie on your back in a large, ring-shaped machine. This scan takes 30-60 minutes, and you must remain as still as possible during this time. This appointment requires you to take at least a half-day off work. 
Resolution	<ul style="list-style-type: none"> Two days after the PET/CT, you are told that no sign of pancreatic cancer was detected. There were about 23 days from the time you received results from the first screening to the results from the PET-CT scan. For these 23 days, it was uncertain whether you might have cancer.
Timeline	

Procedures

- Participants first completed an introductory ranking task. Then, participants valued the health states in a TTO task with a one-year time horizon. After completing the TTO portion of the interview, the participants also completed a demographic and clinical information form.
- Diagnostic pathways for lung, colorectal, breast, and pancreatic cancer were developed. Participants who would not be screened for breast cancer did not value breast cancer health states. Participants who would be screened for breast cancer valued all 10 health states, while the other participants only valued seven.

RESULTS

Figure 2. Mean Health State Utilities*



*Breast cancer health states were only presented to participants who stated that they are or would be screened for breast cancer. Therefore, for the A, B, C, and E health states, N = 203. For the D health states, N = 102.

Sample Description

- A total of 203 participants completed the TTO utility elicitation (see demographics in Table 1).

Table 1. Demographic Characteristics (N=203)

Demographic Characteristics	Descriptive Statistics
Age (mean [SD], years)	42.0 (13.8)
Min age (years)	18
Max age (years)	82
Gender (n, %)	
Male	101 (49.8%)
Female	99 (48.8%)
Non-binary	3 (1.5%)
Ever been screened for cancer ¹ (n, %)	
Lung	2 (1.0%)
Colorectal	13 (6.4%)
Breast	24 (11.8%)
Cervical	36 (17.7%)
Pancreatic	5 (2.5%)
Other	15 (7.4%)
None	134 (66.0%)

¹Not mutually exclusive

Table 2. Mean Health State Utility Values (N=203)

Health States	Follow-up Procedures Described in Health State	Number of Days of Uncertainty about Cancer Diagnosis, as Described in Health State	Disutility of Each FP Experience (i.e., utility difference from health state A)
A. Cancer screening with negative result	-	-	-
B1. False positive for lung cancer without head or neck involvement	CT scan	10	-0.04
B2. False positive for lung cancer with possible head or neck involvement	CT scan; PET-CT	25	-0.10
B3. False positive for lung cancer with a follow-up scan	CT scan	185	-0.11
C. False positive for colorectal cancer	Colonoscopy	14	-0.08
D1. False positive for breast cancer; no biopsy performed	Mammogram/Ultrasound (at same visit)	10	-0.03
D2. False positive for breast cancer; biopsy performed	Mammogram/Ultrasound/Biopsy (at same visit)	10	-0.06
D3. False positive for breast cancer; MRI performed	Mammogram/Ultrasound (at same visit); MRI	20	-0.07
E1. False positive for pancreatic cancer; follow-up CT scan	CT scan	9	-0.05
E2. False positive for pancreatic cancer; follow-up PET-CT	CT scan; PET-CT	23	-0.09

Health State Rankings

- Health state A (true negative) was ranked highest by 98.5% of participants. Reasons that some participants did not rank health state A highest included a desire to undertake the follow-up tests to feel more confident about the negative results.
- For participants ranking the breast cancer health states, health state D1 (FP for breast cancer; no biopsy performed) was most commonly ranked highest among the FP health states (40.2%). For participants who did not rank the breast cancer health states, health state E1 (FP for pancreatic cancer; follow-up CT scan) was most commonly ranked highest among the FP health states (37.6%). In both groups, health state B3 (FP for lung cancer; follow-up CT scan at six months) was most commonly ranked as the least preferred health state (41.2% and 50.5%, respectively).

Health State Utilities

- Mean (SD) utilities are presented in Figure 2 and Table 2. As expected, health state A (true negative) had the highest utility at 0.96 (0.07). Among the FP health states, “FP for breast cancer; no biopsy performed” was the highest with a utility of 0.93 (0.06), and “FP for lung cancer; follow-up CT scan at six months” was the lowest with a utility of 0.85 (0.14).
- When compared to the base health state, “FP for breast cancer; no biopsy performed” had the smallest disutility (-0.03 [0.05]), and “FP for lung cancer; follow-up CT scan at six months” had the largest disutility (-0.11 [0.14]).

CONCLUSIONS

- In general, utilities followed logical patterns, with greater disutility associated with longer duration of uncertainty about the cancer diagnosis and greater perceived severity of the suspected cancer.
- Because the follow-up procedures were added to health states valued with a one-year time horizon, the disutilities can be applied in cost-utility analyses as quality-adjusted life year decrements for each type of FP.
- One inherent limitation of all vignette-based utility elicitation studies is that the resulting utilities are based on perceptions of the health states rather than personal experience.⁴
- Another limitation of the current vignette study is that there is considerable variability of patient experience with these procedures. Therefore, timelines described in the health states may not be applicable to all patients. Timelines were developed using the best judgment of the study team, based on published literature and interviews with cancer screening experts.
- Utilities gathered in this study may be useful in cost-effectiveness analyses examining the value of various methods of cancer screening.

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Disclosures

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