

**Supplement for *Pharmacoeconomics* - Open**

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

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## **HEALTH STATE A: Cancer screening with negative result**

### **Cancer Screening**

- As part of a routine health check, you are **screened for cancer**.

### **Screening Result**

- You are told that **no sign of cancer was detected**.

## **HEALTH STATE B1: False positive for lung cancer without head or neck involvement**

### **Cancer Screening**

- As part of a routine health check, you are **screened for cancer**.

### **Screening Result**

- The screening **results suggest you may have lung cancer**. Therefore, more testing is needed.

### **CT Scan**

- You attend an appointment for a **scan of your chest (called a CT scan)**. This scan will create an **image of your lungs**.
- 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**.
  - In preparation for this scan, you receive an **intravenous (IV) injection of dye** (called contrast), which helps create a **more detailed image of your lungs**.
    - 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.
  - You may have to **hold your breath** for a **few seconds** during the actual scan.
- This appointment requires you to take a **few hours off work**. This scan takes place about **one week** after receiving your initial screening results.

### **Resolution**

- **Two to seven days** after the CT scan, you are told that **no sign of lung cancer was detected**.
- There were about 10 days from the time you received results from the first screening to the results from the follow-up test. **For these 10 days, it was uncertain whether you might have cancer**.

## **HEALTH STATE B2: False positive for lung cancer with possible head or neck involvement**

### **Cancer Screening**

- As part of a routine health check, you are **screened for cancer**.

### **Screening Result**

- The screening **results suggest you may have lung cancer or another type of cancer in your head, neck or chest area**. Therefore, more testing is needed.

### **CT Scan**

- You attend an appointment for a **scan of your chest (called a CT scan)**. This scan will create an **image of your lungs**.
- 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**.
  - In preparation for this scan, you receive an **intravenous (IV) injection of dye** (called contrast) which helps create a **more detailed image of your lungs**.
    - 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.
  - You may have to **hold your breath** for a **few seconds** during the actual scan.
- This appointment requires you to take a **few hours off work**. This scan takes place about **one week** after receiving your initial screening results.
- This scan is **inconclusive**, and **further testing** is recommended.

### **PET/CT Scan**

- About 2 weeks after the CT scan, 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**.
- You may not eat any sugar for 24 hours before the scan.
- The full procedure takes about **four hours**.
  - Prior to the scan, you receive an **intravenous (IV) injection of radioactive sugar** which helps create a **more detailed image of your lungs**.
    - 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

- **Two to seven days** after the PET-CT scan, you are told that **no sign of lung cancer was detected**.
- There were about 25 days from the time you received results from the first screening to the results from the final follow-up test. **For these 25 days, it was uncertain whether you might have cancer.**

## HEALTH STATE B3: False positive for lung cancer with a 6-month follow-up scan

### Cancer Screening

- As part of a routine health check, you are **screened for cancer**.

### Screening Result

- The screening **results** find a spot on your lung, but this is unlikely to be cancer. Spots like this are nearly always harmless.
- To be certain this spot is not cancer, it is recommended that you get **a follow-up scan in six months**.

### CT Scan 6 Months Later

- **Six months later**, you get the follow-up scan (called a **CT scan**). You attend an appointment for a **scan of the target area**. This scan will create an image of **your lungs**.
- The scan itself takes **a few minutes**. During this time, you **lie on your back** in a **large, ring-shaped machine**.
- You may have to **hold your breath** for a **few seconds** during the actual scan.
- This appointment requires you to take a **few hours off work**

### Resolution

- **Two to seven days** after the CT scan, you are told that **no sign of lung cancer was detected**.
- There were about **6 months** from the time you received results from the first screening to the results from the follow-up test. **For these 6 months, you thought it was unlikely that you had cancer, but you were not completely sure.**

## HEALTH STATE C: False positive for colorectal cancer

### Cancer Screening

- As part of a routine health check, you are **screened for cancer**.

### Screening Result

- The screening **results suggest you may have colorectal cancer, which means cancer of the colon or rectum**. Therefore, more testing is needed.

### Colonoscopy

- Your doctor recommends a **colonoscopy**. The procedure is scheduled for **two weeks** after your initial screening.
- **The night before** your procedure, you **drink a liquid that causes significant diarrhea for most of the night**, along with other symptoms like cramping and nausea.
- The **day of your procedure**, you **cannot eat or drink anything except water before the procedure**.
- During the colonoscopy procedure, you are given sedation and pain relief delivered through an intravenous (IV) needle.
  - This means that a **needle is inserted** into a vein in your arm, and fluid flows into your body to keep you comfortable and help you relax during the procedure.
  - If you would prefer not to receive sedation and pain relief, you can have either “gas and air” or no pain relief.
- During the procedure, **a long, flexible tube is inserted into your colon**. A tiny video camera at the tip of the tube allows the doctor to view the inside of the colon. A biopsy may be performed during the procedure.
- You stay at hospital for about 2 hours to make sure you do not have any lingering reaction to the sedation. You need somebody to **drive you to and from the appointment**.
- This appointment requires you to take a **day off work**.

### Resolution

- **Immediately** after the colonoscopy, you are told that **no sign of colorectal cancer was detected**.
- There were about **14 days** from the time you received results from the first screening to the colonoscopy that found no sign of cancer. **For these 14 days, it was uncertain whether you might have cancer**.

## **HEALTH STATE D1: False positive for breast cancer; no biopsy or MRI**

### **Cancer Screening**

- As part of a routine health check, you are **screened for cancer**.

### **Screening Result**

- The screening **results suggest you may have breast cancer**. Therefore, more testing is needed.

### **Mammogram and Ultrasound**

- About **one week** after receiving your screening results, you attend a second appointment for **a diagnostic mammogram and a breast ultrasound** to further examine your breast with imaging. These may be performed during the same visit.
- During the **mammogram**, your **breast is gradually compressed** between **two horizontal plates** while you hold still.
  - The mammogram takes **20-30 minutes** and may cause some discomfort. The breast compression only lasts for a few seconds at a time, and then the top plate is lifted so you can change position.
- During the **ultrasound**, the technician will apply a warm, water-based gel to your breast.
- The gel will help the transducer make secure contact with the body. The transducer is a small handheld plastic device that will be placed gently on your skin. The procedure takes **15 minutes**.

### **Resolution**

- **Three to five days** after your scans, you are told that **no sign of breast cancer was detected**.
- There were about 10 days from the time you received results from the first screening to the results from the follow-up mammogram. **For these 10 days, it was uncertain whether you might have cancer**.

## **HEALTH STATE D2: False positive for breast cancer; biopsy performed**

### **Cancer Screening**

- As part of a routine health check, you are **screened for cancer**.

### **Screening Result**

- The screening **results suggest you may have breast cancer**. Therefore, more testing is needed.

## Mammogram and Ultrasound

- About **one week** after receiving your screening results, you attend a second appointment for **a diagnostic mammogram and a breast ultrasound** to further examine your breast with imaging. These may be performed during the same visit.
- During the **mammogram**, your **breast is gradually compressed** between **two horizontal plates** while you hold still.
  - The mammogram takes **20-30 minutes** and may cause some discomfort. The breast compression only lasts for a few seconds at a time, and then the top plate is lifted so you can change position.
- During the **ultrasound**, the technician will apply a warm, water-based gel to your breast.
- The gel will help the transducer make secure contact with the body. The transducer is a small handheld plastic device that will be placed gently on your skin. The procedure takes **15 minutes**.

## Biopsy

- The mammogram and ultrasound reveal a **suspicious finding** in your breast, so your doctor recommends a **biopsy**. This is done at the same appointment after the mammogram and ultrasound.
  - In a **biopsy**, a **small amount of breast tissue is removed and examined** to determine if it is cancerous.
- **You are awake** for this procedure, but a small amount of your **breast is numbed** so that you **cannot feel any pain**.
- A **small cut** (about half a centimeter) is made in your breast, and a **needle is inserted** in the numbed area so that a **small amount of tissue can be removed**.
- A **small bandage** is applied to the area afterwards. No stitches are necessary. After the procedure, you have some soreness in your breast for about 2 days and bruising near the biopsy site.
- This procedure takes **30-60 minutes**, and your doctor recommends against strenuous physical activity for the remainder of the day.

## Resolution

- **Three to five days** after your biopsy, you are told that **no sign of breast cancer was detected**.
- There were about 10 days from the time you received results from the first screening to the results from the follow-up mammogram and biopsy. **For these 10 days, it was uncertain whether you might have cancer**.

## HEALTH STATE D3: False positive for breast cancer; MRI performed

### Cancer Screening

- As part of a routine health check, you are **screened for cancer**.

### Screening Result

- The screening **results suggest you may have breast cancer**. Therefore, more testing is needed.

### Mammogram and Ultrasound

- About **one week** after receiving your screening results, you attend a second appointment for a **diagnostic mammogram and a breast ultrasound** to further examine your breast with imaging. These may be performed during the same visit.
- During the **mammogram**, your **breast is gradually compressed** between **two horizontal plates** while you hold still.
  - The mammogram takes **20-30 minutes** and may cause some discomfort. The breast compression only lasts for a few seconds at a time, and then the top plate is lifted so you can change position.
- During the **ultrasound**, the technician will apply a warm, water-based gel to your breast.
- The gel will help the transducer make secure contact with the body. The transducer is a small handheld plastic device that will be placed gently on your skin. The procedure takes **15 minutes**.

### MRI Scan

- **Three to five days** later, you are told that **the results of the mammogram and ultrasound were inconclusive, and you are referred for a breast MRI scan**.
- This scan takes place about **one week** after receiving your mammogram and ultrasound results.
- You attend an appointment for a **more detailed scan of your chest (called an MRI)**. This scan will create a more detailed image of **your breast tissue**.
  - The MRI takes about **30 minutes**, during which time you **lie on your stomach** on a table that slides into a **tube-shaped machine**.
  - In preparation for this scan, you receive an **intravenous (IV) injection of dye** (contrast material) which helps create a **more detailed image**.
    - 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.
- While you are lying still in the narrow tube, there are loud noises. This test is **risk-free**, but the tube is relatively **small and enclosed**.



## Resolution

- **Three days** after your MRI, you are told that **no sign of breast cancer was detected**.
- There were about 20 days from the time you received results from the first screening to the results from the follow-up MRI. **For these 20 days, it was uncertain whether you might have cancer.**

## HEALTH STATE E1: False positive for pancreatic cancer; follow-up CT scan

### Cancer Screening

- As part of a routine health check, you are **screened for cancer**.

### Screening Result

- The screening **results suggest you may have pancreatic cancer**. Therefore, more testing is needed.

### CT Scan

- 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**.
  - This liquid may cause mild cramping and diarrhea.
- 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**.
  - 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**.
    - 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.

## Resolution

- **Two days** after the CT scan, you are told that **no sign of pancreatic cancer was detected**.
- There were about 9 days from the time you received results from the first screening to the results from the CT scan. **For these 9 days, it was uncertain whether you might have cancer.**

## HEALTH STATE E2: False positive for pancreatic cancer; follow-up CT scan and PET-CT

### Cancer Screening

- As part of a routine health check, you are **screened for cancer**.

### Screening Result

- The screening **results suggest you may have pancreatic cancer**. Therefore, more testing is needed.

### CT Scan

- 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**.
  - 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**.
  - 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**.
    - 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

- 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**.
  - Prior to the scan, you receive an **intravenous (IV) injection of radioactive sugar** which helps create a **more detailed image of your pancreas**.
    - 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**

- **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.**

## **DECLARATIONS**

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**Competing Interests:** LM, TH, and HK are employed by Evidera, a company that received funding from GRAIL for time spent conducting this research. KC and ETF are employees of GRAIL, LLC, a subsidiary of Illumina, Inc., with equity in Illumina, Inc. MS is a paid consultant to GRAIL. AH is co-investigator for an academic study (SUMMIT) sponsored by UCL, which is funded by GRAIL, has received one honorarium for an advisory board meeting for GRAIL and an honorarium from Evidera Inc. (for this current project), and previously owned shares in Illumina. LN has stock options in Culmination Bio. SJ has received fees for advisory board membership in the last three years from Astra-Zeneca, Bard1 Lifescience, and Johnson and Johnson. He has received grant income from Owlstone and GRAIL Inc. He is an unpaid member of a GRAIL advisory board. He has received lecture fees for academic meetings from Cheisi and Astra Zeneca. His wife works for Astra Zeneca.