

**Follow-up survey conducted Among HIGH-RISK N-NOSE Patients**

**HIROTSU Bio Science Inc. (Head Office: Chiyoda-ku, Tokyo; Representative; Takaaki Hirotsu (Hereinafter referred to as “HIROTSU”)), has conducted a follow-up survey targeted at individuals who were notified of their test results between January and August 2023 using "N-NOSE" and were determined to be at high risk. We are now publishing the first results report of this survey.**

Our company conducted this survey to further facilitate understanding of "N-NOSE" and to ensure that everyone can use it with peace of mind. The survey targeted individuals who used "N-NOSE" between January and August 2023, were notified of their results, and received a high-risk determination. We surveyed 228 individuals who, after receiving their "N-NOSE" results, visited a hospital for further testing, asking whether cancer was actually found. The survey was conducted with the consent of the participants.

Survey Report:

- Out of 228 respondents who went to a hospital for testing following a high-risk determination by "N-NOSE", 47 were diagnosed with cancer.
- Over 65% of those diagnosed with cancer were discovered at stage 0 or 1.
- About 50% of those diagnosed with cancer were found to have abnormalities through endoscopy or MRI.

In this survey, out of 228 individuals who received a high-risk determination from "N-NOSE" and went to a hospital for cancer testing, 47 (20.6%) were actually found to have cancer. While this survey is not a clinical study and thus the results are not intended to explain the accuracy of "N-NOSE", the positive hit rate of general cancer screenings (the probability of finding cancer after being referred for a detailed examination) is reported to be about 1~5%\*<sup>1</sup> for comparison. Additionally, as mentioned in the testimonials, it was found that the high-risk determination from "N-NOSE", even without any symptoms, led to behavioral changes that resulted in early cancer detection upon receiving further examination at a hospital. Furthermore,

it was discovered that most of the cancers were identified by tests such as endoscopy and MRI, which are generally regarded as capable of early detection, indicated by findings.

\*1 Calculated based on "Cancer Registration & Statistics" from the National Cancer Center Cancer Information Service (detection and positive hit rate).

For more detailed survey results, please refer to the "Survey Summary" below. Our company will continue to strive to provide information so that everyone can use our services with confidence.

**Survey target:**

- Those who used N-NOSE and were notified of their test results between January and August 2023 and were judged to be at high risk.

**Number of respondents:**

- 228 items

**Investigation method:**

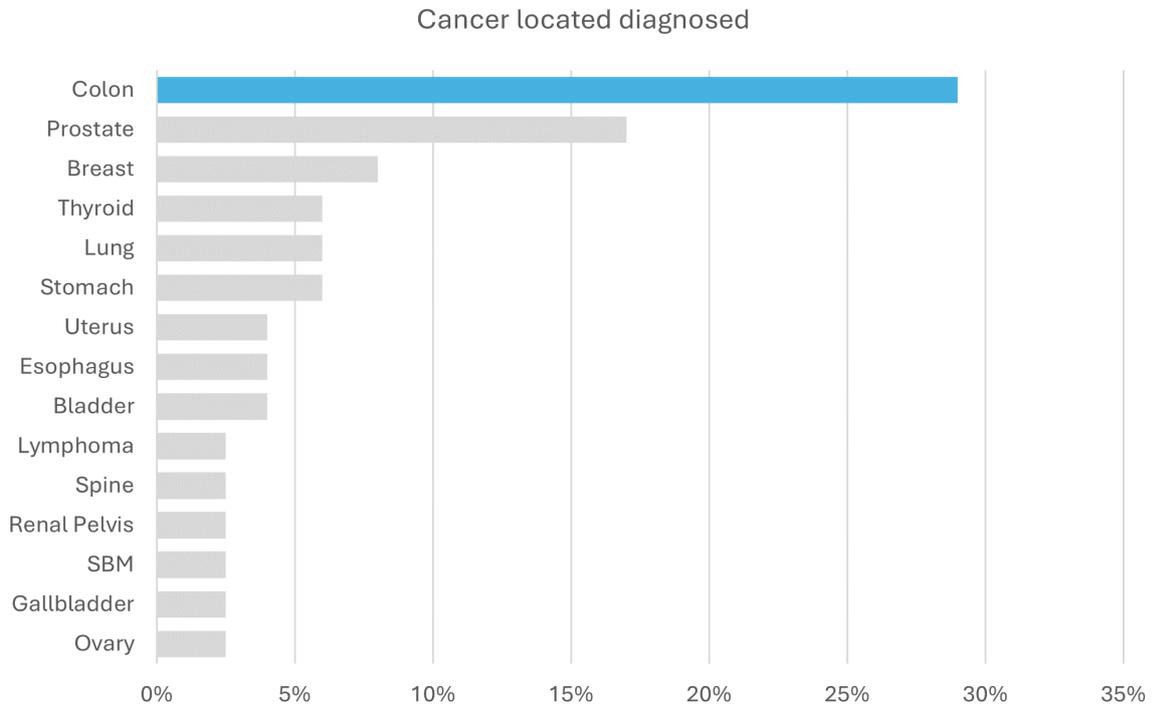
- Internet survey, telephone survey, interviews

**Survey items:**

1. Cancer locations diagnosed
2. Cancer stage at diagnosis
3. Tests taken after taking the N-NOSE test (multiple answers allowed)
4. Test type responsible for successful cancer diagnosis
5. Testimonials from users

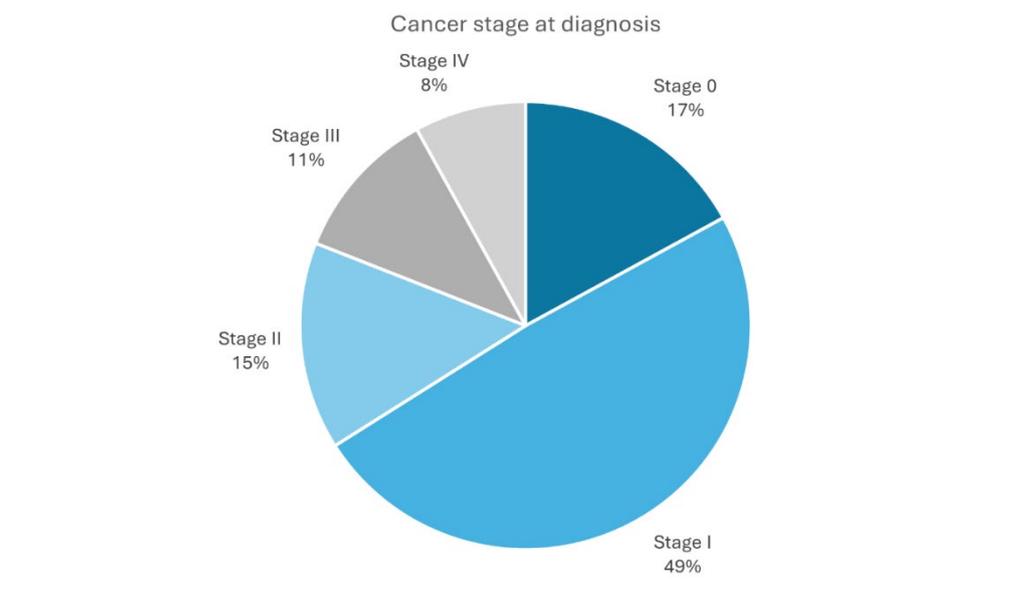
## ■ Survey results

### 1. Cancer locations diagnosed

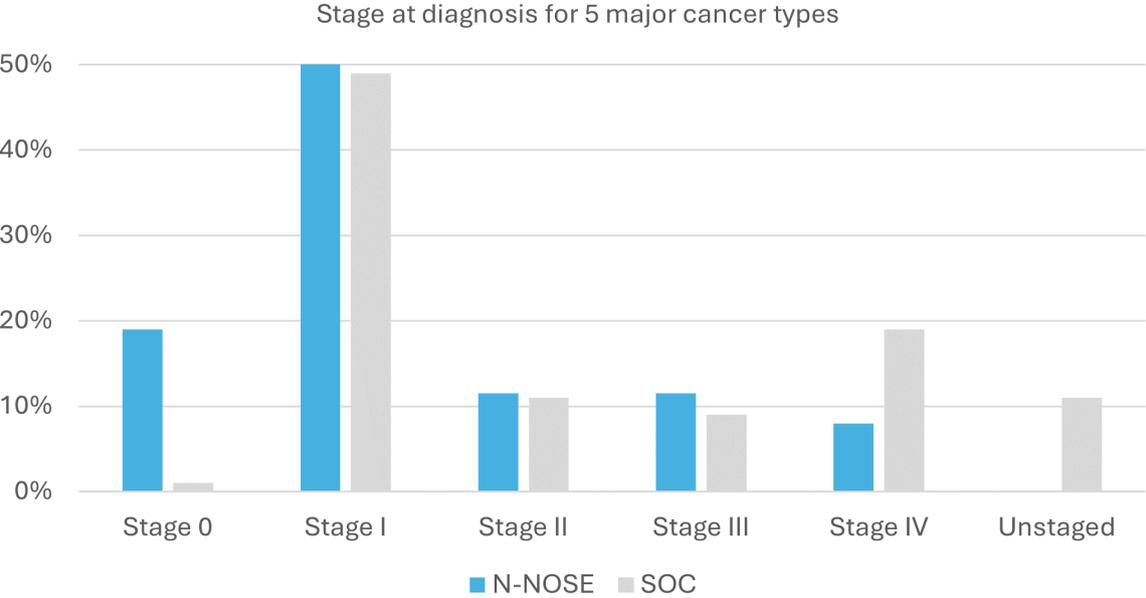


Following a high-risk determination from N-NOSE, the most common site diagnosed with cancer after hospital testing was the colon.

### 2. Cancer stage at diagnosis



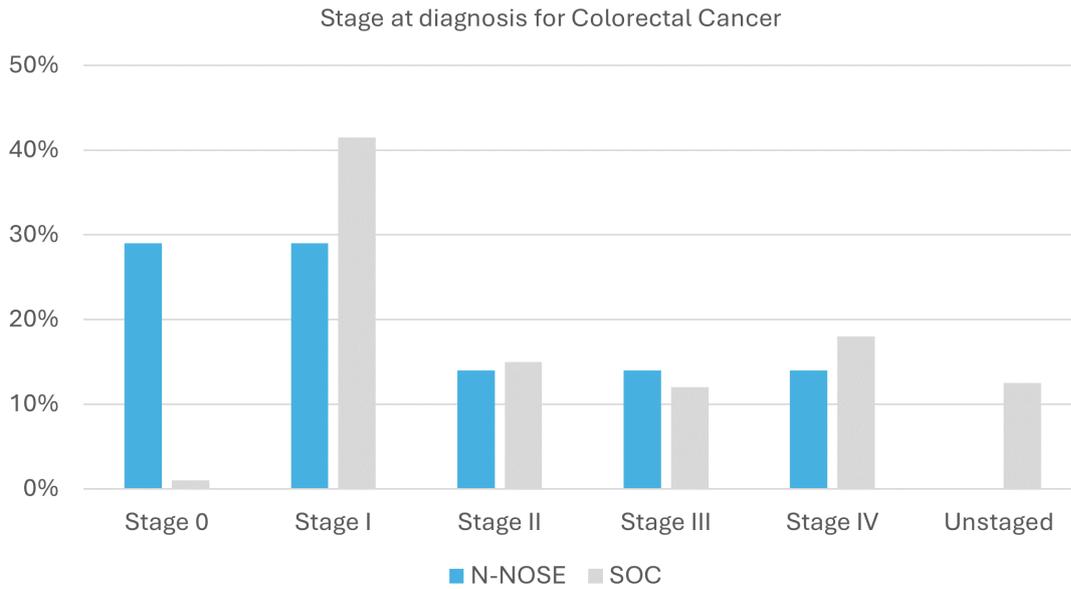
More than 65% of the individuals who received a confirmed diagnosis of cancer after undergoing testing in a hospital following a high-risk determination from N-NOSE were found to be at stage 0 or 1.



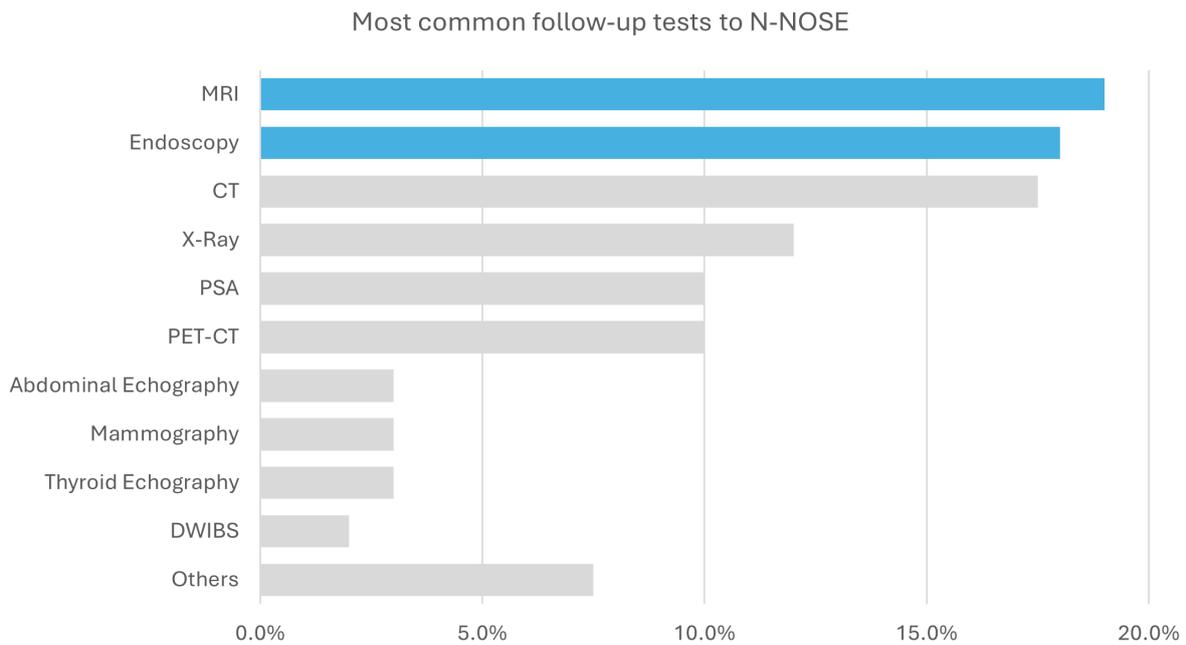
When focusing on the five major cancers, approximately 70% were discovered at stage 0 or 1. Compared to the proportions of each stage at the time of confirmed cancer diagnosis for the five major cancers reported by the Ministry of Health, Labour and Welfare\*2, it was found that individuals with a high-risk determination from N-NOSE had a higher percentage of early detection, especially at stage 0.

\*2 [厚生労働省健康局がん・疾病対策課「全国がん登録 罹患数・率 報告 2019」](#)

Next, when focusing on colon cancer, which had the highest number of reports, the results showed a higher number of detections at stage 0 or 1, especially at stage 0, compared to the report from the Cancer and Disease Control Division of the Health Bureau, Ministry of Health, Labour and Welfare.

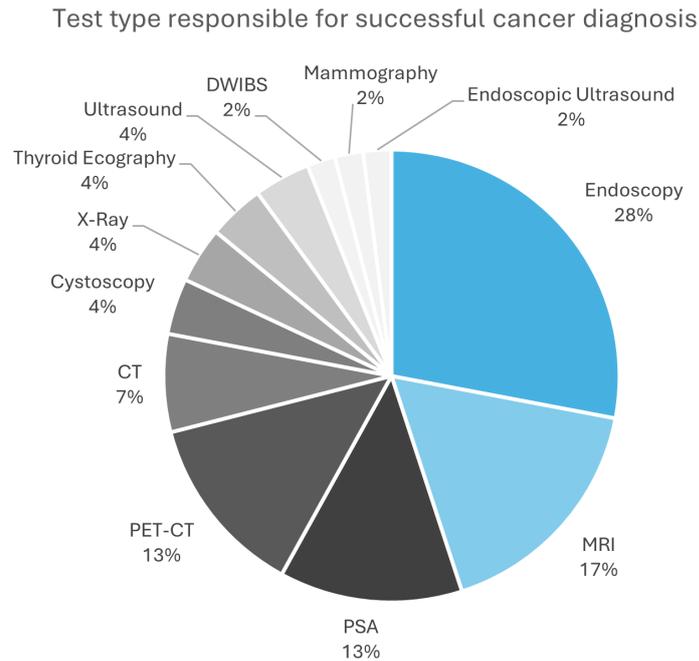


### 3. Tests taken after taking the N-NOSE test (multiple answers allowed)



Regarding the tests that users underwent at hospitals after receiving a high-risk determination from N-NOSE, there was a high occurrence of MRI, endoscopy, and CT scans.

### 4. Test type responsible for successful cancer diagnosis



It was found that nearly 50% of individuals were determined to have findings through endoscopy or MRI after undergoing the N-NOSE examination. Endoscopy, which is said to enable early detection, had the highest frequency among these tests.

## 5. Testimonials from users

- Women / Breast Cancer

Fifteen years ago, I underwent surgery for early-stage breast cancer, and since then, I've been getting annual breast examinations. However, I hadn't had a comprehensive medical check-up for over ten years, so I decided to try N-NOSE because it seemed simple, requiring only a urine sample. The result was a high-risk determination. Around that time, I was also experiencing stomach issues, so I received endoscopic examinations for both my stomach and colon, but those results showed no problems. This made me worry if there could be an issue elsewhere, so when I showed my primary care doctor the N-NOSE results, they became concerned and suggested that it might be a good idea to have a CT scan done. The CT scan revealed incredibly faint, mist-like spots on both lungs and my shoulders, and ultimately, a cytology exam confirmed that it was a metastasis from breast cancer. I had been getting yearly scans, but those were only mammography of the breast. So, I'm truly grateful that I took the N-NOSE test. If I hadn't, I believe I wouldn't have undergone any further examinations. Now, my condition has miraculously improved with treatment. I really would like to recommend N-NOSE to others.

## Male / Stomach Cancer

I have taken the N-NOSE test twice, and this year I received a high-risk determination for the second time. I have been getting endoscopic examinations for my stomach and colon every other year, and this year was supposed to be for the colonoscopy. However, due to the N-NOSE results, I decided to also have a gastroscopy. Then they found a slightly concerning area and suggested that it be removed and sent for a biopsy, which resulted in a diagnosis of early-stage stomach cancer. I had no symptoms, and the decision to have the gastroscopy earlier than planned next year was prompted by the N-NOSE test.

Currently, I am in the stage of practicing eating, but I am also able to practice golf. If I had waited until next year to have the gastroscopy as initially planned, the cancer might have advanced to a further stage. I consider myself lucky that it was discovered this time.

In addition to this survey, our company also publishes testimonials from customers who have actually used "N-NOSE."

<https://lp.n-nose.com/voice/>

### ■ About HIROTSU Bio Science

We as HIROTSU aim to protect the health and future security of people through research, development, and practical application of unique technology that utilize the capabilities of living organisms. Established in 2016, N-NOSE was put into practical use thanks to our researchers' abundance of ideas and tireless efforts. Despite the importance of extending healthy life expectancy being emphasized, it is said that one in every two people will be diagnosed with cancer in this age of 100-year life expectancy. We strive to contribute to solving these social issues with our groundbreaking "bio-diagnoses" technology that utilizes the power of nematodes.

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Headquarters : 22F New Otani Garden Court, 4-1 Kioi-cho, Chiyoda-ku, Tokyo  
Representative : Takaaki Hirotsu, CEO  
Date of Establishment: August 2016  
Main Service : Research, development, and marketing of cancer screenings using nematodes and nematode olfactory sensors  
Official Website : <https://hbio.jp/en/>

■ About “N-NOSE”

A primary screening test for cancer that utilizes the highly accurate detection of cancer-specific odors in human urine by the nematode *C. elegans*, which has a very good sense of smell. By simply submitting urine, the test is simple, inexpensive, highly accurate, and provides a whole-body comprehensive examination of early-stage cancer risk.

Official Service Website: <https://lp.n-nose.com/>

■ About “N-NOSE plus Pancreas”

N-NOSE's next-generation "Cancer Type Specific Test". This test uses a "special nematode" genetically engineered from the nematode *C. elegans* that specifically reacts only to the smell of pancreatic cancer. This "special nematode" has a high ability to distinguish between pancreatic cancer and other cancers, enabling non-invasive detection of early-stage pancreatic cancer.

Official Service Website: <https://lp.n-nose.com/suizou/>

■ About “N-NOSE Animals”

“N-NOSE Dogs” and “N-NOSE Cats” developed based on the N-NOSE technology. Up until now, there has not been an easily accessible cancer screening test for pets. Just like N-NOSE for humans, starting in 2023, an easy cancer risk screening only requiring urine for both cats and dogs has been made available due to this product.

Official Service Website: <https://lp.n-nose.com/animal/>

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