



Lung Cancer Risk Assessment Test

LungSign™ - A New Tool for the Early Detection of Lung Cancer

About LungSign™

LungSign™ is a sputum test assessing individual risk of lung cancer. The test analyzes nuclear features of thousands of sputum cells to render a score that is highly correlated with the presence of lung malignancy. LungSign™ offers improvement over current standards of care and performs similarly for all stages of lung cancer (including carcinoma in situ). Furthermore, with a low rate of false positives, LungSign™ is useful as a complementary test to CT or x-ray.

Indications for Use

LungSign™ is indicated for the evaluation of patients over 50 years old suspicious for lung cancer due to their:

- Significant smoking history (one pack a day for 20 years) or exposure to industrial carcinogens
- Symptomology or clinical suspicion of lung cancer

Exemptions

Caution should be used in the production of sputum where patients have severe cardiovascular trouble or conditions that increase the likelihood of bronchoconstriction (e.g. severe asthma). The following patients should **not** attempt to produce sputum:

- those who have had thoracic or cardiac surgery within the last 6 months
- those with asthma or COPD exacerbation in last 5 days
- those with flu-like symptoms such as fever or chills

LungSign™ Features

- More sensitive than cytology for early stage
- More specific than CT
- Simple, non-invasive

What LungSign™ Measures

LungSign™ is based on the automated analysis of epithelial cells present in a sputum specimen. The test measures properties of cell nuclei such as DNA content, shape, and nuclear chromatin distribution. It identifies possible malignant cells (reported independently) as well as changes in normal appearing cell nuclei that are associated with the presence of malignancy. Available nuclear information is combined into a single score for the specimen.

LungSign™ Results

LungSign™ analysis results in a score typically reported to the physician in 3-5 working days from sample receipt. LungSign™ provides quantitative measure of nuclear abnormality correlated with the presence of lung malignancy. Higher scores suggest an increased likelihood of the presence of lung cancer.

How to order LungSign™

Three easy methods:

1. By phone (toll-free): 1.888.629.8779
2. By email: info@LungSign.com
3. Online: www.LungSign.com

Note: A physician's requisition is required. The cost of the test is CAD\$175.



Interpretation Guide

LungSign™ is not meant to be used as a stand alone test for lung cancer. It should be interpreted in conjunction with recognized diagnostic procedures for the management of patients at risk of lung cancer or undergoing post-surgical follow-up.

Patients with lung malignancies may have low scores. If a patient has relevant symptoms, further investigation is suggested.

Scores fall into three categories as shown in Table 1. These categories are graphically illustrated in Figure 2, where the increase or decrease in the likelihood of the presence of malignancy is shown as a function of score.²

Table 1. LungSign™ score ranges and corresponding interpretations with regard to likelihood of the presence of malignancy.

LungSign™ Score	Interpretation
<3.9	Decreased likelihood of malignancy
3.9—4.6	Result indeterminate for increased or decreased likelihood of malignancy
>4.6	Increased likelihood of malignancy

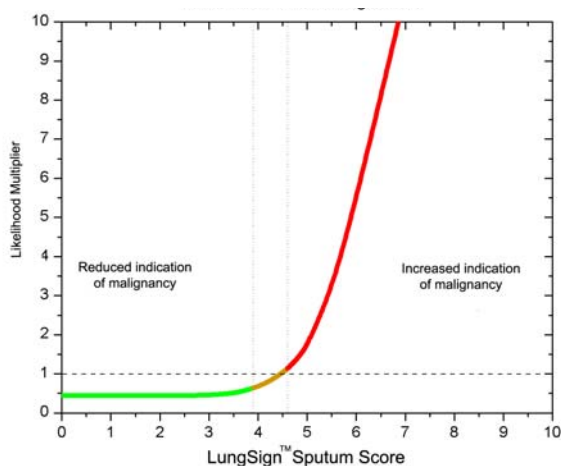


Figure 2. Approximate likelihood ratio multipliers for the odds of harboring lung cancer as a function of LungSign™ score. The likelihood multiplier updates the patient's post-test risk of lung cancer. It should be interpreted in the context of the relevant lung cancer risk factors and symptoms which specify the patient's pre-test likelihood of harboring the disease. The red segment represents increased likelihood (scores > 4.6) and the green segment represents decreased likelihood (scores < 3.9), with scores in between (orange) considered indeterminate. For example, with a LungSign™ score of 6 the likelihood that the patient harbors a malignancy is increased by more than 5 times.

Pre-test Risk for Screening Population (0.5-2%)

In a screening population consisting of asymptomatic individuals at risk of lung cancer due to age (over 50 years) plus heavy smoking (over 20 pack years) or carcinogen exposure, the disease prevalence may be between 0.5 – 2%.

Pre-test Risk for Very High Risk Population (10%)

The additional presence of symptoms (such as persistent cough or shortness of breath) raise the likelihood of lung cancer and place the patient in a prevalence group that may be 10% or higher.

Table 2 shows estimates³ of the LungSign™ predictive values (i.e. the probability of malignancy corresponding to a particular test score) for the 2% and 10% disease-prevalence groups.

Table 2. Interpretation Guide: Estimates³ of the probability of malignancy for LungSign™ scores for different patient populations.

LungSign™ score	Probability of malignancy ⁴	
	Screening population (2% prevalence)	Very high risk population (10% prevalence)
1	1	5
2	1	5
3	1	5
3.9	1	7
4	1	7
4.6	2	11
5	3	16
6	10	38
≥7	≥18	≥54

It may be difficult to categorize the patient's pre-test risk, and it is therefore suggested that patients with high scores and those with low scores but suspicious symptomology be referred for further evaluation.

Notes:

- LungSign™ is a test based on ClearSign™ technology.
- The performance claims of LungSign™ were established using induced sputum samples.
- LungSign™ performance was determined through a blinded clinical trial where the test was prospectively applied to participants who were suspicious for lung cancer. A total of 986 participants with analyzable specimens were included, of whom 330 were determined by conventional means to have lung cancer. The empirically observed performance was 91% specificity and 40% sensitivity for a LungSign™ score threshold of 5.
- LungSign™ was studied in a group of patients in the care of lung cancer specialists where the lung cancer prevalence was 33%. The predictive values shown in Table 2 are estimates based on an extension of the test to lower disease-prevalence patient groups and should only be used for general guidance—they are not exact values for either prevalence group.