# Women with Breast Cancer, Especially Those Who Received Chemotherapy, at Increased Risk for Subsequent Lung Cancer

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## Key Findings:

- Primary lung cancer is more than twice as prevalent in women previously diagnosed with breast cancer compared to women who have not had breast cancer.
- Women who had breast cancer and received chemotherapy have the greatest risk of subsequent primary lung cancer with a 57% increase in risk compared to those who received radiation and a 171% increase in risk compared to those who received endocrine therapies.

Breast cancer is the most diagnosed cancer in women.[1] One study found that in the 10 years following their initial breast cancer diagnosis, around 10% of patients are diagnosed with a second primary cancer.[2] However, less is known about what factors, such as type of cancer treatment, might contribute to the development of these second primary cancers.

To better understand how breast cancer and second primary lung cancer might be correlated, we studied 2,071,295 women aged 50–84 who received a screening mammogram between 2010 and 2023. Patients with an elevated breast cancer risk as evidenced by a previous breast or lung cancer diagnosis, a screening less than three months prior, or starting screening mammograms prior to age 50 were excluded. We assessed the rate of primary lung cancer in the five years following the screening mammogram among patients who received a breast cancer diagnosis and compared it with the rate of lung cancer in patients who did not receive a breast cancer diagnosis. We found that the five-year risk of lung cancer was doubled in the patients with breast cancer compared to those without, as shown in Figure 1.

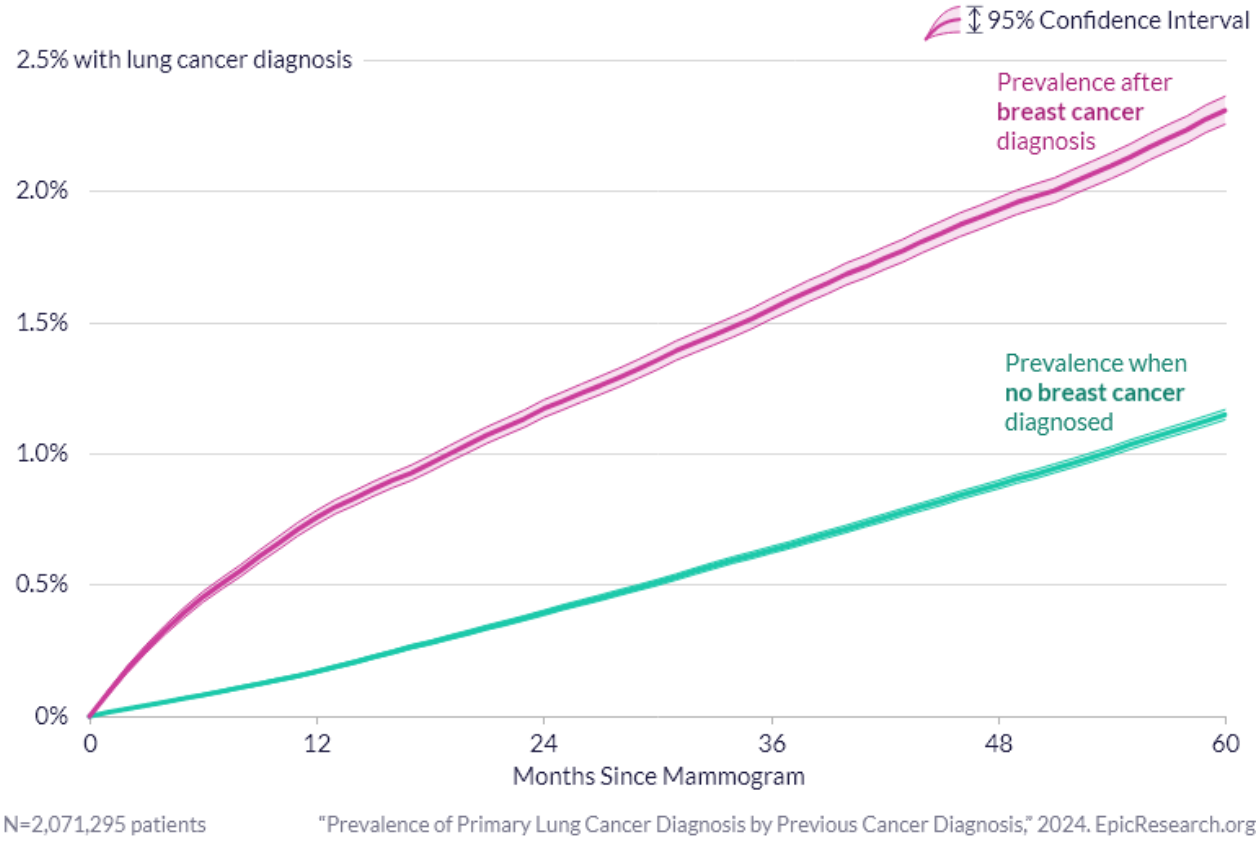


*Figure 1. Prevalence of primary lung cancer diagnosis by month for five years following screening exam, stratified by breast cancer status.*

We then further stratified the breast cancer population by the type of treatment received following the breast cancer diagnosis. Patients who received multiple forms of treatment are included in each category. We found that breast cancer patients who received chemotherapy were the most likely to be diagnosed with subsequent primary lung cancer compared to breast cancer patients who received radiation or endocrine therapies, as shown in Figure 2. A sensitivity analysis using a Cox proportional hazards model yielded similar results.

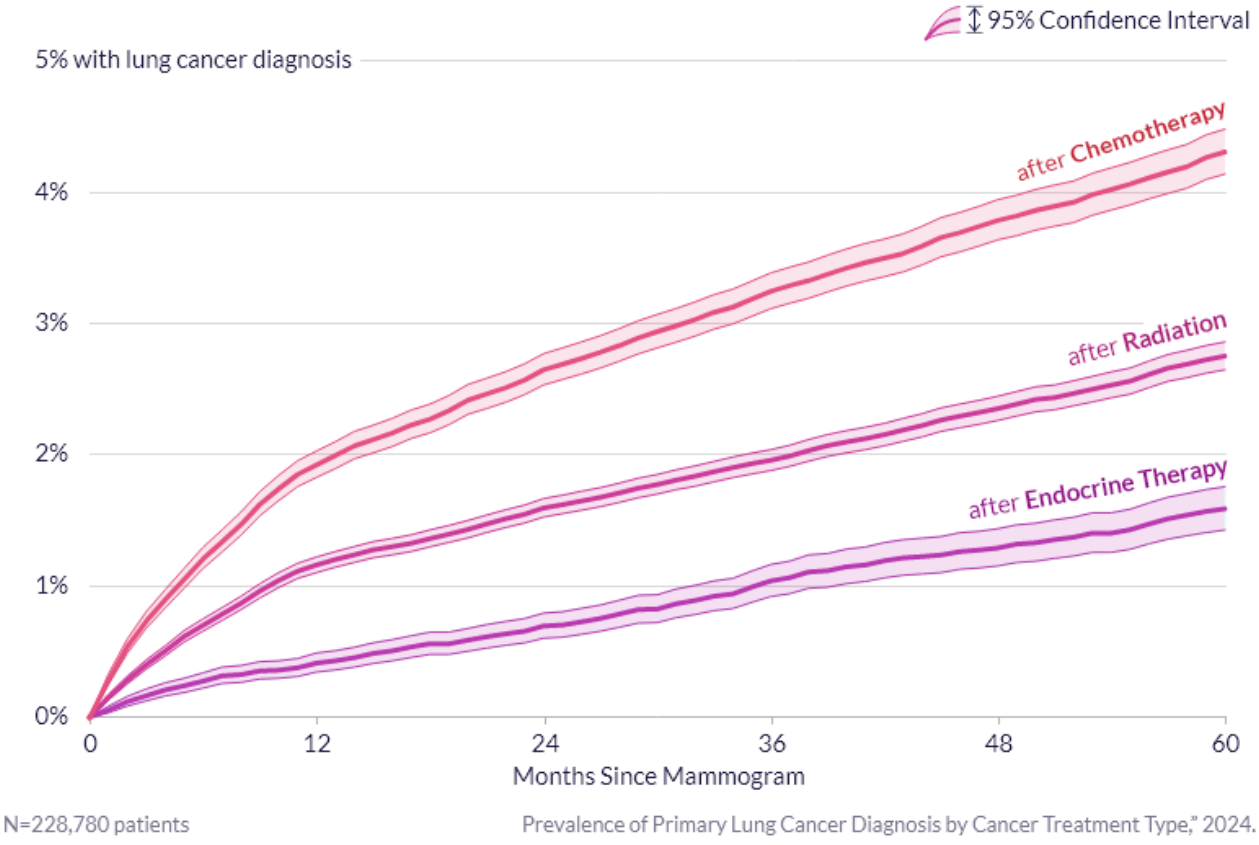


*Figure 2. Prevalence of lung cancer diagnosis by month for five years following screening exam, stratified by breast cancer treatment type.*

These findings suggest that patients diagnosed with breast cancer are at an increased risk of developing second primary lung cancer. Additional monitoring, such as lung cancer screening, may be warranted in patients with a previous history of breast cancer, especially if previous treatment included chemotherapy.

*These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 243 million patient records from 1,400 hospitals and more than 32,500 clinics from all 50 states and Lebanon. This study was completed in collaboration with researchers from Rush University Medical Center and Vanderbilt University Medical Center. This study was completed by two teams that worked independently, each composed of clinicians and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.*

## References


1. Wang R, Yin Z, Liu L, et al. Second Primary Lung Cancer After Breast Cancer: A Population-Based Study of 6,269 Women. *Front Oncol.* 2018;8:427. Published 2018 Oct 9. doi:10.3389/fonc.2018.00427
2. Hayat MJ, Howlader N, Reichman ME, Edwards BK. Cancer statistics, trends, and multiple primary cancer analyses from the Surveillance, Epidemiology, and End Results (SEER) Program. *Oncologist.* 2007;12(1):20-37. doi:10.1634/theoncologist.12-1-20


## Data Definitions

| Term | Definition |
|---|---|
| **Study period** | Breast cancer screenings between 1/1/2010 and 1/17/2023 |

| | |
|---|---|
| **Study population** | Patients with a breast cancer screening:<br>Age 50-84 at screening<br>Female legal sex<br>No lung cancer or breast cancer prior to screening<br>No screening in the past 90 days<br>All screenings from patients starting before age 50 were excluded<br><br>**Breast Cancer Screening**:<br>Diagnosis of:<br>ICD-10-CM code Z12.31 or R92*<br>ICD-9-CM code V76.1*<br>SNOMED CT code 268547008, 24623002, 384151000119104, 71651007, or 129714008<br>Procedure of:<br>CPT 76641, 76642, 76981, 76982, 76983, 77046, 77047, 77048, 77049, 77051, 77052, 77055, 77056, 77057, 77063, 77065, 77066, 77067<br>HCPCS G0202, G0204, G0206, G0279<br>ICD-9-CM Vol 3 87.37<br>Epic procedures IMG588, IMG589, IMG600, IMG605, IMG608, IMG609, IMG617, IMG621, IMG669, IMG670, IMG671<br>Procedure or lab component of LOINC 24597-7, 24604-1, 24605-8, 24606-6, 24610-8, 26175-0, 26176-8, 26177-6, 26287-3, 26289-9, 26291-5, 26346-7, 26347-5, 26348-3, 26349-1, 26350-9, 26351-7, 36319-2, 36625-2, 36626-0, 36627-8, 36642-7, 36962-9, 37005-6, 37006-4, 37016-3, 37017-1, 37028-8, 37029-6, 37030-4, 37037-9, 37038-7, 37052-8, 37053-6, 37539-4, 37542-8, 37543-6, 37551-9, 37552-7, 37553-5, 37554-3, 37768-9, 37769-7, 37770-5, 37771-3, 37772-1, 37773-9, 37774-7, 37775-4, 38070-9, 38071-7, 38072-5, 38079-0, 38080-8, 38090-7, 38091-5, 38095-6, 38096-4, 38807-4, 38820-7, 38821-5, 38825-6, 38854-6, 38855-3, 39054-2, 39145-8, 39146-6, 39147-4, 39148-2, 39150-8, 39152-4, 39153-2, 39154-0, 42132-1, 42168-5, 42169-3, 42174-3, 42415-0, 42416-8, 42680-9, 46335-6, 46336-4, 46337-2, 46338-0, 46339-8, 46342-2, 46350-5, 46351-3, 46352-1, 46354-7, 46355-4, 46356-2, 46380-2, 48475-8, 48492-3, 49509-3, 49510-1, 69150-1, 69159-2, 69251-7, 69259-0, 69268-1, 72137-3, 72138-1, 72139-9, 72140-7, 72141-5, 72142-3, 86348-0, 86349-8, 86350-6, 86359-7, 86360-5, 86367-0, 86368-8, 86369-6, 86370-4, 86416-5, 86462-9, 86463-7, 91517-3, 91518-1, 91519-9, 91520-7, 91521-5, 91522-3 |
| **Exposures** | **Breast Cancer** within 1 year of the screening<br>Diagnosis of ICD-10-CM C50* or D05*<br>Diagnosis of ICD-9-CM 174*<br><br>**Radiation therapy** within 1 year of the screening<br>Diagnosis of ICD-10-CM Z51.0 or Z92.3<br>Diagnosis of ICD-9-CM V58.0 or V15.3<br>Diagnosis of SNOMED CT 108290001, 429479009 |

| | |
|---|---|
| | Procedure of CPT code 19294, 19296-19298, 77371-77373, 77385-77387, 77401-77416, 77422-77425, 77750, 77520, 77522-77525, 77761-77763, 77767, 77768, 77789, 77790, 77770-77772, 77778, 0395T<br>Procedure of HCPCS code G6001-G6017, Q3001<br>Procedure of ICD-10-PCS DM*, 0HHT_1*, 0HHU_1*, 0HHV_1*, 0HHW_1*, 0HHX_1*<br>Procedure of ICD-9-CM Vol 3 92.2*<br><br>**Chemotherapy** within 1 year of screening<br>Diagnosis of ICD-10-CM Z51.1* or Z92.21<br>Diagnosis of ICD-9-CM V58.1* or V87.41<br>Diagnosis of SNOMED CT 367336001 or 161653008<br>Procedure of CPT 96401-96417, 96420-96425<br>Procedure HCPCS code G0498, G2206, G9829, Q0083-Q0085, S9329-S9331<br>Procedure of ICD-9-CM Vol 3 00.10<br><br>**Endocrine Therapy** within 1 year of screening<br>Order for a medication with a pharmaceutical subclass of:<br>Antineoplastic – Selective Estrogen Receptor Degraders (SERDs)<br>Antineoplastic - Selective Estrogen Receptor Modulators (SERMs)<br>Antineoplastic – LHRH (GnRH) Agonist Analog Pituitary Suppressants<br>Antineoplastic – Aromatase Inhibitors |
| **Outcomes** | **Lung Cancer**<br>ICD-10-CM C34* or D02.2*<br>ICD-9-CM 162.2-162.5, 162.8, 162.9 |
| **Model Specifications** | Kaplan Meier and Cox PH<br>Censor as of lung cancer identification or most recent outpatient F2F encounter |
| **Patient matching** | We matched each patient diagnosed with breast cancer to 4 patients not diagnosed with breast cancer based on screening year, smoking status, patient age, race, and ethnicity. |

## Figure 1. Prevalence of Primary Lung Cancer Diagnosis by Previous Cancer Diagnosis

| Month | Breast Cancer - Survival Rate | CI Lower Subtract | CI Upper Add | No Breast Cancer - Survival Rate | CI Lower Subtract | CI Upper Add |
|---|---|---|---|---|---|---|
| **0** | 1.000 | 0.000 | 0.000 | 1.000 | 0.000 | 0.000 |
| **1** | 0.999 | 0.000 | 0.000 | 1.000 | 0.000 | 0.000 |
| **2** | 0.998 | 0.000 | 0.000 | 1.000 | 0.000 | 0.000 |
| **3** | 0.997 | 0.000 | 0.000 | 1.000 | 0.000 | 0.000 |
| **4** | 0.997 | 0.000 | 0.000 | 0.999 | 0.000 | 0.000 |
| **5** | 0.996 | 0.000 | 0.000 | 0.999 | 0.000 | 0.000 |
| **6** | 0.995 | 0.000 | 0.000 | 0.999 | 0.000 | 0.000 |
| **7** | 0.995 | 0.000 | 0.000 | 0.999 | 0.000 | 0.000 |
| **8** | 0.994 | 0.000 | 0.000 | 0.999 | 0.000 | 0.000 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **9** | 0.994 | 0.000 | 0.000 | 0.999 | 0.000 | 0.000 |
| **10** | 0.993 | 0.000 | 0.000 | 0.999 | 0.000 | 0.000 |
| **11** | 0.993 | 0.000 | 0.000 | 0.998 | 0.000 | 0.000 |
| **12** | 0.992 | 0.000 | 0.000 | 0.998 | 0.000 | 0.000 |
| **13** | 0.992 | 0.000 | 0.000 | 0.998 | 0.000 | 0.000 |
| **14** | 0.992 | 0.000 | 0.000 | 0.998 | 0.000 | 0.000 |
| **15** | 0.991 | 0.000 | 0.000 | 0.998 | 0.000 | 0.000 |
| **16** | 0.991 | 0.000 | 0.000 | 0.998 | 0.000 | 0.000 |
| **17** | 0.991 | 0.000 | 0.000 | 0.997 | 0.000 | 0.000 |
| **18** | 0.990 | 0.000 | 0.000 | 0.997 | 0.000 | 0.000 |
| **19** | 0.990 | 0.000 | 0.000 | 0.997 | 0.000 | 0.000 |
| **20** | 0.990 | 0.000 | 0.000 | 0.997 | 0.000 | 0.000 |
| **21** | 0.989 | 0.000 | 0.000 | 0.997 | 0.000 | 0.000 |
| **22** | 0.989 | 0.000 | 0.000 | 0.996 | 0.000 | 0.000 |
| **23** | 0.989 | 0.000 | 0.000 | 0.996 | 0.000 | 0.000 |
| **24** | 0.988 | 0.000 | 0.000 | 0.996 | 0.000 | 0.000 |
| **25** | 0.988 | 0.000 | 0.000 | 0.996 | 0.000 | 0.000 |
| **26** | 0.988 | 0.000 | 0.000 | 0.996 | 0.000 | 0.000 |
| **27** | 0.987 | 0.000 | 0.000 | 0.995 | 0.000 | 0.000 |
| **28** | 0.987 | 0.000 | 0.000 | 0.995 | 0.000 | 0.000 |
| **29** | 0.987 | 0.000 | 0.000 | 0.995 | 0.000 | 0.000 |
| **30** | 0.986 | 0.000 | 0.000 | 0.995 | 0.000 | 0.000 |
| **31** | 0.986 | 0.000 | 0.000 | 0.995 | 0.000 | 0.000 |
| **32** | 0.986 | 0.000 | 0.000 | 0.994 | 0.000 | 0.000 |
| **33** | 0.985 | 0.000 | 0.000 | 0.994 | 0.000 | 0.000 |
| **34** | 0.985 | 0.000 | 0.000 | 0.994 | 0.000 | 0.000 |
| **35** | 0.985 | 0.000 | 0.000 | 0.994 | 0.000 | 0.000 |
| **36** | 0.984 | 0.000 | 0.000 | 0.994 | 0.000 | 0.000 |
| **37** | 0.984 | 0.000 | 0.000 | 0.993 | 0.000 | 0.000 |
| **38** | 0.984 | 0.000 | 0.000 | 0.993 | 0.000 | 0.000 |
| **39** | 0.983 | 0.000 | 0.000 | 0.993 | 0.000 | 0.000 |
| **40** | 0.983 | 0.000 | 0.000 | 0.993 | 0.000 | 0.000 |
| **41** | 0.983 | 0.000 | 0.000 | 0.993 | 0.000 | 0.000 |
| **42** | 0.983 | 0.000 | 0.000 | 0.992 | 0.000 | 0.000 |
| **43** | 0.982 | 0.000 | 0.000 | 0.992 | 0.000 | 0.000 |
| **44** | 0.982 | 0.000 | 0.000 | 0.992 | 0.000 | 0.000 |
| **45** | 0.982 | 0.000 | 0.000 | 0.992 | 0.000 | 0.000 |
| **46** | 0.981 | 0.000 | 0.000 | 0.992 | 0.000 | 0.000 |
| **47** | 0.981 | 0.000 | 0.000 | 0.991 | 0.000 | 0.000 |
| **48** | 0.981 | 0.000 | 0.000 | 0.991 | 0.000 | 0.000 |
| **49** | 0.980 | 0.000 | 0.000 | 0.991 | 0.000 | 0.000 |

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|---|---|---|---|---|---|---|
| **50** | 0.980 | 0.000 | 0.000 | 0.991 | 0.000 | 0.000 |
| **51** | 0.980 | 0.000 | 0.000 | 0.991 | 0.000 | 0.000 |
| **52** | 0.980 | 0.000 | 0.000 | 0.990 | 0.000 | 0.000 |
| **53** | 0.979 | 0.000 | 0.000 | 0.990 | 0.000 | 0.000 |
| **54** | 0.979 | 0.000 | 0.000 | 0.990 | 0.000 | 0.000 |
| **55** | 0.979 | 0.001 | 0.000 | 0.990 | 0.000 | 0.000 |
| **56** | 0.978 | 0.001 | 0.000 | 0.989 | 0.000 | 0.000 |
| **57** | 0.978 | 0.001 | 0.001 | 0.989 | 0.000 | 0.000 |
| **58** | 0.978 | 0.001 | 0.001 | 0.989 | 0.000 | 0.000 |
| **59** | 0.977 | 0.001 | 0.001 | 0.989 | 0.000 | 0.000 |
| **60** | 0.977 | 0.001 | 0.001 | 0.989 | 0.000 | 0.000 |

## Figure 2. Prevalence of Primary Lung Cancer Diagnosis by Cancer Treatment Type

| Month | Radiation - Survival Rate | CI Lower Subtract | CI Upper Add | Chemotherapy - Survival Rate | CI Lower Subtract | CI Upper Add | Endocrine Therapy - Survival Rate | CI Lower Subtract | CI Upper Add |
|---|---|---|---|---|---|---|---|---|---|
| **0** | 1.000 | 0.000 | 0.000 | 1.000 | 0.000 | 0.000 | 1.000 | 0.000 | 0.000 |
| **1** | 0.998 | 0.000 | 0.000 | 0.997 | 0.000 | 0.000 | 0.999 | 0.000 | 0.000 |
| **2** | 0.997 | 0.000 | 0.000 | 0.995 | 0.001 | 0.001 | 0.999 | 0.000 | 0.000 |
| **3** | 0.996 | 0.000 | 0.000 | 0.993 | 0.001 | 0.001 | 0.998 | 0.001 | 0.000 |
| **4** | 0.995 | 0.000 | 0.000 | 0.991 | 0.001 | 0.001 | 0.998 | 0.001 | 0.000 |
| **5** | 0.994 | 0.000 | 0.000 | 0.989 | 0.001 | 0.001 | 0.998 | 0.001 | 0.000 |
| **6** | 0.993 | 0.000 | 0.000 | 0.988 | 0.001 | 0.001 | 0.997 | 0.001 | 0.001 |
| **7** | 0.992 | 0.001 | 0.000 | 0.987 | 0.001 | 0.001 | 0.997 | 0.001 | 0.001 |
| **8** | 0.991 | 0.001 | 0.000 | 0.985 | 0.001 | 0.001 | 0.997 | 0.001 | 0.001 |
| **9** | 0.990 | 0.001 | 0.001 | 0.984 | 0.001 | 0.001 | 0.996 | 0.001 | 0.001 |
| **10** | 0.990 | 0.001 | 0.001 | 0.983 | 0.001 | 0.001 | 0.996 | 0.001 | 0.001 |
| **11** | 0.989 | 0.001 | 0.001 | 0.981 | 0.001 | 0.001 | 0.996 | 0.001 | 0.001 |
| **12** | 0.988 | 0.001 | 0.001 | 0.981 | 0.001 | 0.001 | 0.996 | 0.001 | 0.001 |
| **13** | 0.988 | 0.001 | 0.001 | 0.980 | 0.001 | 0.001 | 0.996 | 0.001 | 0.001 |
| **14** | 0.988 | 0.001 | 0.001 | 0.979 | 0.001 | 0.001 | 0.995 | 0.001 | 0.001 |
| **15** | 0.987 | 0.001 | 0.001 | 0.979 | 0.001 | 0.001 | 0.995 | 0.001 | 0.001 |
| **16** | 0.987 | 0.001 | 0.001 | 0.978 | 0.001 | 0.001 | 0.995 | 0.001 | 0.001 |
| **17** | 0.987 | 0.001 | 0.001 | 0.978 | 0.001 | 0.001 | 0.995 | 0.001 | 0.001 |
| **18** | 0.986 | 0.001 | 0.001 | 0.977 | 0.001 | 0.001 | 0.994 | 0.001 | 0.001 |
| **19** | 0.986 | 0.001 | 0.001 | 0.977 | 0.001 | 0.001 | 0.994 | 0.001 | 0.001 |
| **20** | 0.986 | 0.001 | 0.001 | 0.976 | 0.001 | 0.001 | 0.994 | 0.001 | 0.001 |
| **21** | 0.985 | 0.001 | 0.001 | 0.975 | 0.001 | 0.001 | 0.994 | 0.001 | 0.001 |
| **22** | 0.985 | 0.001 | 0.001 | 0.975 | 0.001 | 0.001 | 0.994 | 0.001 | 0.001 |
| **23** | 0.985 | 0.001 | 0.001 | 0.974 | 0.001 | 0.001 | 0.993 | 0.001 | 0.001 |

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|---|---|---|---|---|---|---|---|---|---|
| **24** | 0.984 | 0.001 | 0.001 | 0.974 | 0.001 | 0.001 | 0.993 | 0.001 | 0.001 |
| **25** | 0.984 | 0.001 | 0.001 | 0.973 | 0.001 | 0.001 | 0.993 | 0.001 | 0.001 |
| **26** | 0.984 | 0.001 | 0.001 | 0.973 | 0.001 | 0.001 | 0.993 | 0.001 | 0.001 |
| **27** | 0.983 | 0.001 | 0.001 | 0.972 | 0.001 | 0.001 | 0.992 | 0.001 | 0.001 |
| **28** | 0.983 | 0.001 | 0.001 | 0.972 | 0.001 | 0.001 | 0.992 | 0.001 | 0.001 |
| **29** | 0.983 | 0.001 | 0.001 | 0.971 | 0.001 | 0.001 | 0.992 | 0.001 | 0.001 |
| **30** | 0.982 | 0.001 | 0.001 | 0.971 | 0.001 | 0.001 | 0.992 | 0.001 | 0.001 |
| **31** | 0.982 | 0.001 | 0.001 | 0.970 | 0.001 | 0.001 | 0.991 | 0.001 | 0.001 |
| **32** | 0.982 | 0.001 | 0.001 | 0.970 | 0.001 | 0.001 | 0.991 | 0.001 | 0.001 |
| **33** | 0.981 | 0.001 | 0.001 | 0.969 | 0.001 | 0.001 | 0.991 | 0.001 | 0.001 |
| **34** | 0.981 | 0.001 | 0.001 | 0.969 | 0.001 | 0.001 | 0.991 | 0.001 | 0.001 |
| **35** | 0.981 | 0.001 | 0.001 | 0.968 | 0.001 | 0.001 | 0.990 | 0.001 | 0.001 |
| **36** | 0.980 | 0.001 | 0.001 | 0.968 | 0.001 | 0.001 | 0.990 | 0.001 | 0.001 |
| **37** | 0.980 | 0.001 | 0.001 | 0.967 | 0.001 | 0.001 | 0.989 | 0.001 | 0.001 |
| **38** | 0.980 | 0.001 | 0.001 | 0.967 | 0.001 | 0.001 | 0.989 | 0.001 | 0.001 |
| **39** | 0.979 | 0.001 | 0.001 | 0.966 | 0.001 | 0.001 | 0.989 | 0.001 | 0.001 |
| **40** | 0.979 | 0.001 | 0.001 | 0.966 | 0.001 | 0.001 | 0.989 | 0.001 | 0.001 |
| **41** | 0.979 | 0.001 | 0.001 | 0.965 | 0.001 | 0.001 | 0.988 | 0.001 | 0.001 |
| **42** | 0.978 | 0.001 | 0.001 | 0.965 | 0.001 | 0.001 | 0.988 | 0.001 | 0.001 |
| **43** | 0.978 | 0.001 | 0.001 | 0.965 | 0.001 | 0.001 | 0.988 | 0.001 | 0.001 |
| **44** | 0.978 | 0.001 | 0.001 | 0.964 | 0.001 | 0.001 | 0.988 | 0.001 | 0.001 |
| **45** | 0.977 | 0.001 | 0.001 | 0.963 | 0.002 | 0.001 | 0.988 | 0.001 | 0.001 |
| **46** | 0.977 | 0.001 | 0.001 | 0.963 | 0.002 | 0.001 | 0.987 | 0.001 | 0.001 |
| **47** | 0.977 | 0.001 | 0.001 | 0.963 | 0.002 | 0.001 | 0.987 | 0.001 | 0.001 |
| **48** | 0.976 | 0.001 | 0.001 | 0.962 | 0.002 | 0.001 | 0.987 | 0.001 | 0.001 |
| **49** | 0.976 | 0.001 | 0.001 | 0.962 | 0.002 | 0.002 | 0.987 | 0.002 | 0.001 |
| **50** | 0.976 | 0.001 | 0.001 | 0.961 | 0.002 | 0.002 | 0.987 | 0.002 | 0.001 |
| **51** | 0.976 | 0.001 | 0.001 | 0.961 | 0.002 | 0.002 | 0.986 | 0.002 | 0.001 |
| **52** | 0.975 | 0.001 | 0.001 | 0.961 | 0.002 | 0.002 | 0.986 | 0.002 | 0.001 |
| **53** | 0.975 | 0.001 | 0.001 | 0.960 | 0.002 | 0.002 | 0.986 | 0.002 | 0.001 |
| **54** | 0.975 | 0.001 | 0.001 | 0.960 | 0.002 | 0.002 | 0.986 | 0.002 | 0.001 |
| **55** | 0.974 | 0.001 | 0.001 | 0.959 | 0.002 | 0.002 | 0.986 | 0.002 | 0.001 |
| **56** | 0.974 | 0.001 | 0.001 | 0.959 | 0.002 | 0.002 | 0.985 | 0.002 | 0.001 |
| **57** | 0.973 | 0.001 | 0.001 | 0.958 | 0.002 | 0.002 | 0.985 | 0.002 | 0.002 |
| **58** | 0.973 | 0.001 | 0.001 | 0.958 | 0.002 | 0.002 | 0.985 | 0.002 | 0.002 |
| **59** | 0.973 | 0.001 | 0.001 | 0.957 | 0.002 | 0.002 | 0.984 | 0.002 | 0.002 |
| **60** | 0.972 | 0.001 | 0.001 | 0.957 | 0.002 | 0.002 | 0.984 | 0.002 | 0.002 |