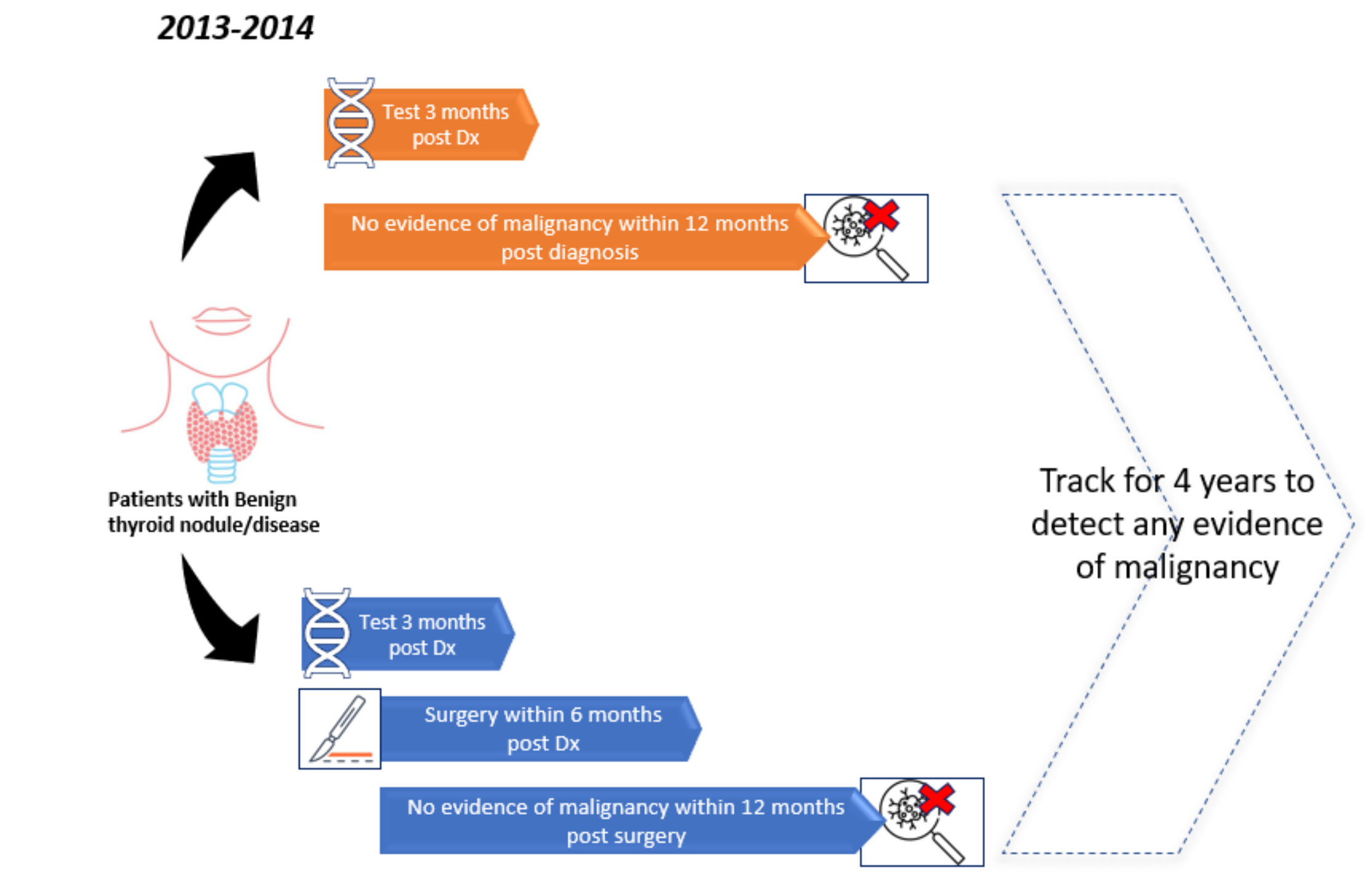


**USE OF MEDICAL CLAIMS DATA TO ASSESS THE IMPACT OF GENOMIC CLASSIFIERS ON UNDERDIAGNOSIS OF MALIGNANCIES OF THE THYROID GLAND VERSUS PERFORMING UNNECESSARY SURGERIES**

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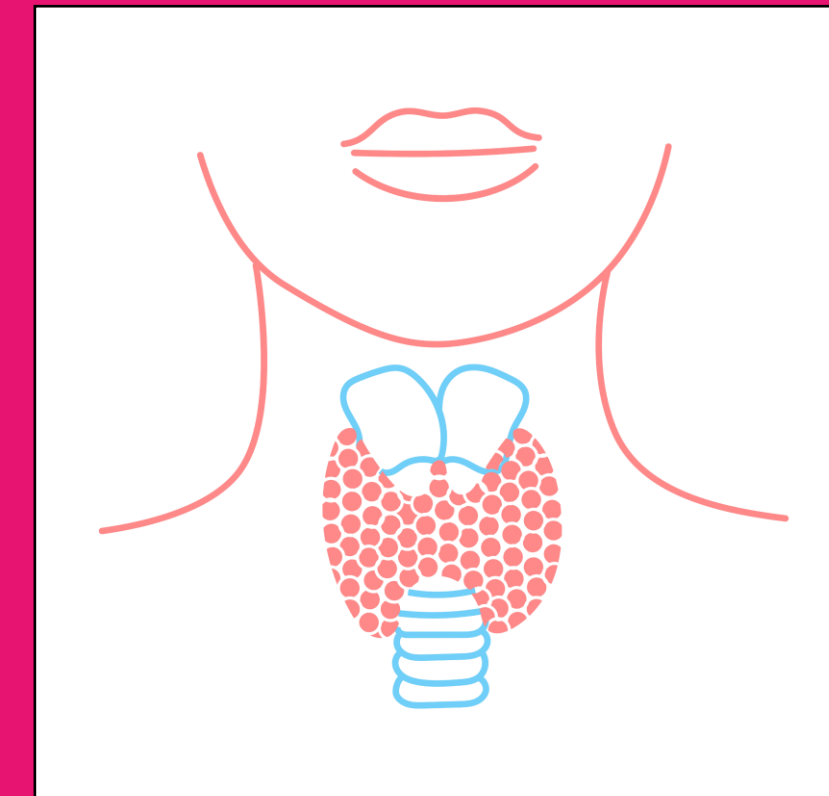
- INTRO**
- 4-7% of adult US population have palpable thyroid nodule. Only 1 of 20 clinically identified nodules is malignant.<sup>1</sup>
  - Genomic classifiers; multigene assays designed to predict malignancy, can return indeterminate posing possibility of under/over performing surgeries with the consequence of either lowering chances of early stage treatment, or incurring unnecessary resources that can impact patient quality of life.
  - The study used claims data to assess impact of genomic classifiers on underdiagnosing thyroid malignancies versus unnecessary surgeries.

- METHODS**
- Study analyzed patients 18 years and older with thyroid benign neoplasms or nodular diseases using ICD-9/10-CM codes [2013-2014]
  - Patients must have evidence of thyroid/Molecular panel within 3 months suggesting treating physician suspected malignancy.
  - Surgery within 6 months post-diagnosis assigned patient to “Surgery arm” and lack thereof assigned patient to “No Surgery arm”.
  - Patients must have no evidence of malignancy 12 months post-diagnosis, and if they had surgery, 12 months post-surgery, suggesting test returned negative/indeterminate.
  - Hazard Ratio to develop malignancy was assessed using Cox Proportional Hazards (CoxPH) method.



- RESULTS**
- 2,982 patients qualified for the study; 83% were females. 49% were initially diagnosed with Non-Toxic Goiter, 25% were under the category that’s defined by ICD9/10 codes as unspecified, 24% had Iodine-Deficiency Goiter and 2% had Benign Neoplasm of Thyroid Gland
  - 89% had no evidence of surgical procedures of thyroid gland and 340 (11%) had evidence of surgical procedures of thyroid gland.

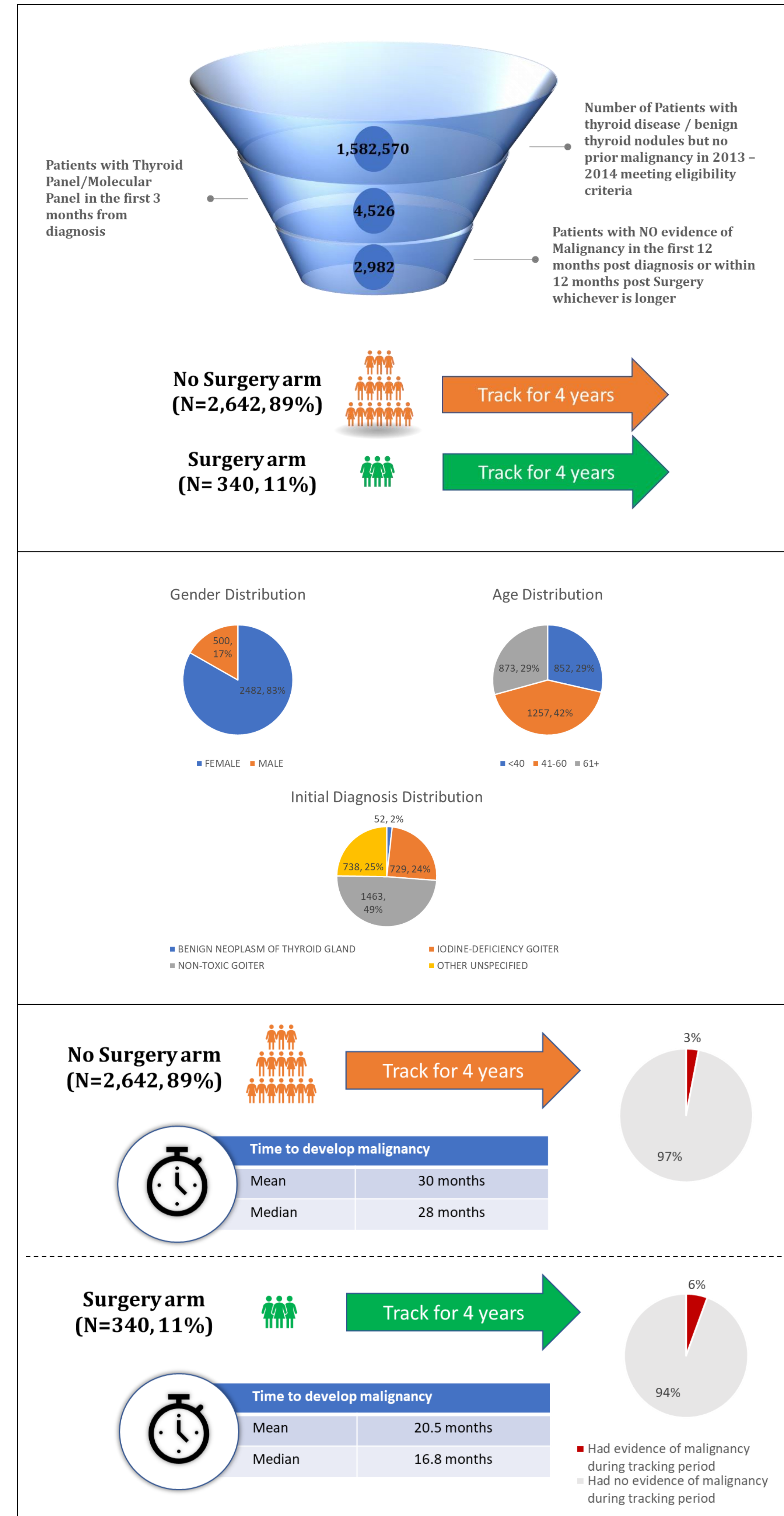
# Sparing Patients With Nodular Thyroid Disease Unnecessary Surgeries Didn't increase their Chances Of Developing Thyroid Malignancies Later.



**PCN245**

- 3% of the patients who didn't have surgery developed malignancy within 30 months on average, with a median of 28 months from initial diagnosis
- On the other hand, 6% of those who had surgery developed malignancy within 20.5 months on average (~10 months less than the no surgery arm) with a median of 17 months as opposed to 28 months in the no surgery arm.

- Discussion**
- Within the overall study population, not performing surgery showed to not increase the chances of developing malignancy later in life as demonstrated by probability to develop malignancy (HR 0.53 (0.32-0.87) P Value: 0.0128). In this study, patients who didn't undergo surgery had lower chance of developing malignancy proving statistically significant non-inferiority to performing surgery at 95% CI level.
  - Probability of developing malignancy with or without surgery varies by age, gender and initial diagnosis with varying range of significance in different subgroup.
  - Age under 40 (HR 0.17 (0.06-0.47)), females (HR 0.53(0.3-0.94)), initial diagnosis of Iodine-Deficiency Goiter (HR 0.29 (0.1-0.79)) showed significant favorability of not undergoing surgery at 95% CI level.
  - Ages 41-60 (HR 0.5 (0.3-0.94)) and Benign Neoplasm of Thyroid Gland (HR 0.12 (0.01-1.34)) showed advantage of not performing surgery although didn't rise to the 95% CI significance. Given the smaller size of the patients in this analysis with an initial diagnosis of Benign Neoplasm of Thyroid Gland, further investigation of these subgroups can be done in following analyses.
  - Ages 61+ showed the highest HR 0.92 (0.39-2.16) with a wide CI despite of the relatively large sample suggesting



that further investigation is needed in this subpopulation.

Subgroup	Hazard Ratio		Hazard Ratio for Malignancy (95% CI)	P Value
	No Surgery no. of Malignancy, of patients	Surgery no. of Malignancy, of patients		
Overall	89/2642	19/340	0.53 (0.32-0.87)	0.0128
Age Group				
0-40	9/813	6/94	0.17 (0.06-0.47)	7e-04
41-60	23/1107	7/158	0.5 (0.22-1.16)	0.1054
61-90	46/722	6/88	0.92 (0.39-2.16)	0.8563
Gender				
Female	65/2224	14/258	0.53 (0.3-0.94)	0.0295
Male	15/418	5/82	0.58 (0.21-1.58)	0.2845
Thyroid Diagnosis Category				
Benign Thyroid Gland	1/41	2/11	0.12 (0.01-1.34)	0.0854
Iodine Deficiency Goiter	15/663	5/66	0.29 (0.1-0.79)	0.0155
Non Toxic Goiter	42/1240	10/223	0.75 (0.37-1.48)	0.403
Other Unspecified	22/658	2/40	0.62 (0.15-2.64)	0.52

- Limitations and Considerations:**
- The study is based on claims data which has a broad coverage of a wide variety of patients, payers and providers, but doesn't provide details around tumor stage, histology or data around new lesions vs recurrence or transformation of old lesions.
  - The Genomic test in the analysis is identified using an NGS or a PCR codes with no knowledge of specific test or genes included; a known shortcoming of claims data. In this analysis we didn't use FISH or IHC tests typically used for point mutations or single aberrations which will not serve the objective of the study. Test results aren't available in claims data, but no evidence of malignancy for 12 months post diagnosis/surgery is a reasonable proof of an indeterminate or benign result report.
  - Although we applied longitudinal visibility rules both in time and geography to ensure full capture of patient activity, data coverage gaps need to be considered in interpreting the data.
  - In interpreting the data, an important consideration is correlation versus causation and reverse causation. Higher rates in Benign Neoplasms can be due to nature and aggressiveness of disease. The study wasn't designed to assess the degree or severity of initial indication or malignancy staging or origin.
  - Another consideration is the details around decision of undergoing surgery vs not by the patient and physician. The decision could have been driven by more suspicious nodules clinically, sonographically or pathologically which can increase risk of malignancy later in life. The study as designed won't be able to provide this distinction. Patient psychology and involvement in the decision are other factors not assessed in the analysis and can have an impact.
  - Small sample size for Benign Neoplasm of Thyroid Gland [N=52] which widened the CI below the 95% level. Further investigation of this subgroup can be done in following analyses.

**References**  
 1.(NEngJMed.2004Oct21;351(17):1764-71.,Clinical practice.The thyroid nodule.)

