# Predicting Cervical Neoplasms Among Intrauterine Device Users

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**Abstract**

*A previous study from the OHDSI community showed that the relative risk of cervical neoplasms is higher for levonorgestrel intrauterine system (LNG-IUS) compared to copper intrauterine device (Cu-IUD) users [1]. The objective of this study is to develop and validate patient-level prediction models for patients in Cu-IUD and LNG-IUS cohorts.*

**Background**

The OHDSI community has presented evidence to suggest that LNG-IUS exposure may double the risk of high grade cervical neoplasms relative to Cu-IUD exposure. These findings may have implications for the health of approximately 1 million women. The purpose of this study is to predict which IUD users may be at risk for developing a cervical neoplasm. A valid prediction model may lead to protective interventions for Cu-IUD or LNG-IUS users who have an elevated risk for high grade cervical neoplasms.

**Methods**

We implemented a retrospective, observational, cohort study. Using ATLAS, we made 3 target cohorts for Cu-IUD users, LNG-IUS users, and all IUD users. The first two target cohorts and outcome cohort have been described previously [1]. Additionally, we made a third target cohort that did not specify LNG-IUS exposure. The time at risk was from 1 year to 10 years after IUD implantation. The prediction was implemented with a Lasso Logistic Regression, among other models at the discretion of the investigators. The study data came from the Truven MarketScan Commercial Claims & Encounters (CCAE) database.

**Results**

The crude incidences of cervical neoplasms for the Cu-IUD and LNG-IUS were similar to the rates reported in the previous study [1] (Table 1). The AUC was 0.7 for the Cu-IUD and all IUD users cohorts. For the LNG-IUS cohort, the model did not converge. Prior HPV infection, synthetic hormone exposure, vaginal delivery and smoking history were associated with a cervical neoplasm (Table 2).

| Target Cohort Name | Target Count | Outcome Count | %Outcome Incidence | AUC |
|---|---|---|---|---|
| Cu-IUD | 124702 | 893 | 0.7 | 0.68 |
| LNG-IUS | 6650 | 94 | 1.4 | N/A |
| IUD All | 126365 | 917 | 0.7 | 0.67 |

**Table 1**: Model performance for the target cohorts. AUC = Area Under the Curve. Cu-IUD = Copper IUD, LNG-IUS = Levonorgestrel Intrauterine System, IUD All = All IUD Users.

| Time Window | Variable | Coefficient |
|---|---|---|
| 365 to 0 days prior | HPV DNA Detection | 0.37 |
| Any to 0 days prior | Levonorgestrel Exposure | 0.35 |
| Any to 0 days prior | Normal delivery | 0.20 |
| 365 to 0 days prior | Etonogestrel Exposure | 0.12 |
| 365 to 0 days prior | Ex-cigarette Smoker | 0.11 |

**Table 2**: Covariates and coefficients for variables associated with the outcome for the Cu-IUD cohort.

## Discussion/Conclusion

The covariates that were associated with a high grade cervical neoplasm were consistent with known risk factors. This finding supports the validity of using OHDSI data to evaluate novel cervical neoplasia risks, such as IUD type.

## References

1. Spotnitz ME, Natarajan K, Ryan PB, Westhoff CL. *Relative Risk of Cervical Neoplasms Among Copper and Levonorgestrel-Releasing Intrauterine Device Users.* Obstet Gynecol 135(2):319-327 (2020).