Project Title:
Evaluation for predictive factors for permanent versus transient hypothyroidism in children diagnosed with congenital hypothyroidism (CH) through the Newborn Screening Ontario (NSO) Program

Background:
Congenital hypothyroidism is an important endocrine condition screened for on newborn screening in many locations word wide. However, its incidence has been noted to increase in many published studies with the thought that this may be due to increased detection of transient CH (T-CH). The consequences of delayed differentiation for those with T-CH include unnecessary medicalization, frequent blood work, daily levothyroxine supplementation, extensive follow-up, and increased use of medical resources. These could be mitigated if transient cases could be identified earlier with earlier trials off treatment.

Project Objectives:
1. To analyze the predictive factors for permanent and transient CH in children who screen positive on newborn screening and are started on treatment.
2. To develop a predictive tool in which individual patient factors (screening TSH, diagnostic TSH, diagnostic FT4, thyroxine dose/kg to maintain normal TSH, thyroid imaging, gestational age, antibody testing) can be used to help determine likelihood of transient CH.

Study Methods
Retrospective cohort study assessing all newborns who screened positive for congenital hypothyroidism in Ontario from April 1, 2006, to September 1, 2015 for whom $\geq$ 3 years of follow-up data was available.

Results
Of 469 cases with confirmed congenital hypothyroidism, 360 (76.8%) were diagnosed with P-CH and 109 (23.2%) with T-CH. Doses of levothyroxine predicting T-CH were <3.9 mcg/kg at 6 months, <3.0 mcg/kg at 1 and 2 years, and <2.5 mcg/kg at 3 years. Thyroid imaging was the strongest individual predictor ($p<0.001$) of P-CH. Without imaging, significant predictors included thyroxine dose/kg ($p<0.001-0.002$), screening TSH ($p=0.03$), rise in TSH above the reference interval on treatment ($p=0.002$), and history of maternal thyroid disease ($p=0.02$). A risk score was developed to identify children with T-CH who may benefit from an earlier trial off therapy at the year mark as this is when the differences between P-CH and T-CH become more significant.

Presentations
1.   Canadian Pediatric Endocrine Group Conference 2021: Poster Presentation
2.   Pediatric Endocrine Society Conference 2021: Oral Presentation

Publication
Alexa Marr, Nicole Yokubynas, Ken Tang, David Saleh, Diane K Wherrett, Robert Stein, Ereny Bassilious, Pranesh Chakraborty, Sarah E Lawrence, Transient Versus Permanent Congenital Hypothyroidism in Ontario, Canada: Predictive Factors and Scoring System, *The Journal of Clinical Endocrinology & Metabolism*, 2021;, dgab798, **Error! Hyperlink reference not valid.**

Goals
Our hope is that this study can be used along with other important publications on this topic to aid in the prediction of patients who may be able to safety undergo an earlier trial off of Levothyroxine therapy, ultimately saving the family and the health care system time and resources. While other publications (see background section of manuscript) list important predictive factors, our study was larger than most and went

a step further to create a predictive scoring tool which will provide a more concrete decision aid for clinicians to use.