Applying Data Preparation Methods to Optimize Preterm Birth Prediction

by

Alana Esty, B. Eng.

A thesis submitted to the Faculty of Graduate and Postdoctoral Affairs in partial fulfillment of the requirements for the degree of

Master of Applied Science

in

Biomedical Engineering

Ottawa - Carleton Institute for Biomedical Engineering (OCIBME)

Carleton University

Ottawa, Ontario

July 2018

Abstract

The purpose of this work was to develop an accurate prediction model which can process information contained in antenatal databases to determine whether a baby will be born prematurely. The focus was on improved data preprocessing to add to methods developed by previous students in the Carleton MIRG (Medical Information technology Research Group) lab.

The machine learning classifiers used included Decision Tree (DT) classifiers (for feature reduction) and the Artificial Neural Network (ANN) classifier (for model evaluation). Missing values and class imbalance was dealt with by applying software packages in the R statistical programming language.

This research has shown a marked improvement in the accuracy of predicting preterm births. The final sensitivity and specificity results for the BORN (Better Outcomes Registry and Network) database were: Parous 89.2%, and 67.8%, Nulliparous 89.0% and 71.5%, and for PRAMS (Pregnancy Risk Assessment Monitoring System) database: Parous 84.1% and 71.4%, Nulliparous 83.8% and 76.0%. These improved results are promising. An accurate predictive tool will allow caregivers to implement preventative treatment strategies or to ensure delivery occurs in a tertiary health care Centre.

Acknowledgements

I would like to thank my thesis supervisor, Dr. Monique Frize, for her support, advice and guidance throughout my degree. Thank you for the opportunity to be exposed to and work on a variety of enriching projects and workshops.

Thank you to my co-supervisor, Dr. Jeff Gilchrist who provided exceptional feedback and mentorship throughout my degree.

Thank you to my co-supervisor, Dr. Erika Bariciak at the Children's Hospital of Eastern Ontario who was always available for questions and provided detailed and relevant feedback and support.

I am also thankful for my parents who have consistently supported me through both the highs and lows of my graduate degree and have always encouraged me to strive for the best I can.

I would also like to thank Guy Kouamou Ntonfo, Carole Love, everyone at the Carleton GSA and of course, Dawn Patrice Collins Gregory, I am very grateful for their support and encouragement.

Table of Contents

List of Tables .....

List of Figures

List of Appendices .....

List of Acronyms

ACC	Accuracy
ANN	Artificial Neural Network
AOM	Association of Ontario Midwives
APGAR	Activity, Pulse, Grimace, Appearance and Respiration
AUC	Area Under Curve
BASH	Bourne-Again Shell
BORN	Better Outcomes Registry Network
BP	Blood Pressure
CBR	Case-Based Reasoning
CCR	Correct Classification Rate
CDC	Centers for Disease Control and Prevention
CDR	Clinical Data Repository
CHEO	Children's Hospital of Eastern Ontario
CL	Cervical Length
CSV	Comma Separated Value
DT	Decision Tree
FANN	Fast Artificial Neural Network
fFN	Fetal Fibronectin
FN	False Negative
FP	False Positive
FS	Feature Selection
NICU	Neonatal Intensive Care Unit
k-NN	k-Nearest Neighbour
LBW	Low Birth Weight
MAR	Missing at Random
MCAR	Missing Completely at Random
MCC	Matthews Correlation Coefficient
MICE	Multivariate Imputation via Chained Equations
MIRG	Medical Information technologies Research Group
MLP	Multilayer Perceptron
MSE	Mean Squared Error
NICU	Neonatal Intensive Care Unit
NMAR	Not Missing at Random
NPV	Negative Predictive Value
OPR	Ontario Perinatal Record
OMA	Ontario Medical Association
PHIPA	Personal Health Information Protection Act
PCMCH	Provincial Council for Maternal Child Health

PBNN	Pruning Based Neural Network
PPADS	Physician-PArent Decision Support
PPV	Positive Predictive Value
PRAMS	Pregnancy Risk Assessment Monitoring System
PTB	Preterm Birth
RFW	Research Framework
ROC	Receiver Operating Curve
SQL	Structured Query Language
TN	True Negative
TP	True Positive
EMG	Uterine Electromyography

1. Chapter: Introduction

The purpose of this introductory chapter is to provide a framework for this thesis, including the motivation for the research from both a healthcare and engineering perspective. In addition, an overview of the problem statement, a description of the clinical environment, preterm birth, the databases used, and the thesis objectives and outline are addressed.

1.1. Motivation

1.1.1. Healthcare Perspective

In the current healthcare environment data is constantly being collected by clinical and hospital equipment. The ability to access massive amounts of healthcare data is a gold mine for predicting future health outcomes [1]. Large companies such as Google, GE Health, and IBM have recognized the potential of these massive datasets and have developed algorithms for recognizing patterns in health data [2]. For instance, Google has developed machine learning algorithms to quickly identify health conditions [3].

This work analyzes two large clinical datasets containing antenatal health information: the Better Outcomes Registry and Network (BORN) Database [4] and the Pregnancy Risk Assessment Monitoring System (PRAMS) Database [5]. Premature birth can have critical long-term effects on the patient, the family and on the clinical environment. From a healthcare perspective, there can be a huge benefit in being able to flag women who might be at risk for preterm birth; this enables the health care team to apply preventative care and to decide how best to manage the delivery. Currently methods used by healthcare teams to try to predict preterm birth are invasive, not very accurate or reliable, and are only used once the patients presents with symptoms of potential preterm [6].

1.1.2. Engineering Perspective

The use of classifiers within the healthcare field is rapidly increasing. The role of software tools when analyzing "Big Data" is that these tools have capabilities to deal with massive amounts of data and can rapidly observe inherent patterns and correlations in clinical data [1]. This can ultimately aid clinicians during prevention, diagnosis and post-diagnosis stages to improve the care provided to patients. "Big Data" can encompass many different definitions, but in the case of this research work, it consists of large databases which contain a variety of patient data and information.

The machine learning techniques used in this thesis work combine both Decision Tree (DT) and Artificial Neural Network (ANN) classifiers to classify neonatal outcomes. The DT classifier implemented the C5.0 RuleQuest Research software [6]. The ANN classifier implemented the Fast-Artificial Neural Network (FANN) library [7]. From an engineering perspective, increasing the accuracy of classifiers to identify health outcomes can assist physicians in make a diagnosis, understanding prognosis, and developing tailored treatment plans.

1.2. Problem Statement

In the past, clinicians would make predictions of a patient's future outcomes based on that individual's medical history. The benefit of using machine learning techniques such as an integrated DT-ANN model, is that software tools can quickly draw upon a multitude of clinical features, resulting, ideally, in a more accurate prediction of outcome for the individual.

Data preprocessing is arguably one of the most important steps in the data mining process [8], [9], [10]. Data preprocessing contains many steps: data cleaning, feature selection, normalization

and transformation of the data. Without this data preprocessing step, model evaluation can result in misleading and inaccurate results [10]. The two datasets analyzed for this research work contain raw, noisy, real-life data which needs to be preprocessed before entering the data into the ANN model.

This thesis represents continuation of work done by previous MIRG students including: Catley, Yu and Ong. Catley developed an early prediction model which used a combination of Multilayer Perceptron Artificial Neural Networks and a decision tree voting algorithm [11]. This hybrid machine learning classifier was then further developed by Yu, who used the decision tree classifier to eliminate variables and then applied an artificial neural network with weight-elimination, with improved sensitivity and specificity results [12]. Finally, Ong's work introduced a new neural network classifier using the Fast-Artificial Neural Network Library [13]. Compared to past research, which focused on the machine learning models, the primary focus of this work is on data preparation to improve the sensitivity metric. The emphasis is on sensitivity, as this performance metric describes the probability of the classifier correctly predicting preterm cases. A prediction model with a high sensitivity will also help to ensure positive cases are not missed. This is important, since the eventual integration of the classifier into a clinical setting will necessitate identification of the risk of preterm birth as early as possible in the pregnancy while not missing any positive cases.

1.3.Clinical Environment

Obstetrics is the area of medicine focused on childbirth and maternal health during childbirth. Preventing and predicting preterm birth is an important area in the field of obstetrics, since preterm birth is associated with decreased infant survival, increased risk for short term and long-term health complications, and an increased use of health care technology and expenses [14].

Tocolytic drugs are medications used to delay the onset of labour [14]. Research shows that there is no evidence that these drugs improve neonatal outcomes and can result in adverse effects for both the mother and baby [14]. Frequently, these drugs are used as a last resort before a preterm birth occurs. The focus of this research work is on predicting preterm birth, because with accurate, non-invasive prediction methods, physicians can apply antenatal interventions as early as possible and potentially improve birth outcome for infants.

1.4.Defining Preterm Birth

Preterm birth is defined as birth which takes place before 37 weeks of gestation [15]. In Ontario, the preterm birth rate is 7.9% [16]. In the US, the frequency of preterm birth is around 8-12% and in other developed nations in Europe the rate is around 5-9% [17]. Often there is no definite identified cause of preterm birth; however, there are several socioeconomic, physiological and environmental factors which can contribute to the risk of a preterm birth [17]. Some of these factors include smoking, having previous children who were premature, and bacterial vaginosis [17]. In addition, the risk of infant mortality with a premature birth is generally quite high [18]. These infants at birth are still in the early stages of development and this can leave them more susceptible to illness and disease. For instance, premature infants often require mechanical ventilation, as their lungs have not fully developed. Many of these infants experience several chronic illnesses such as chronic lung disease and respiratory distress syndrome [19].These high-risk situations can be damaging for the long-term health of the infant and can result in short and long-term costs for hospitals.

The fetal fibronectin test is considered the current gold standard for predicting preterm birth, specifically for women with a history of preterm birth; however, the test is expensive and

invasive [20], [21], [22]. In addition, the sensitivity of the test varies depending on the gestational week and the test can only be used once the patient presents with symptoms which are indicative of potential impending preterm birth [23]. Therefore, a less expensive method which can either meet or exceed the accuracy and timing of the current standard is desired.

1.5. Databases

The PRAMS database contains over 100,000 cases with over 300 general clinical features of state-specific population-based maternal and infant data [5]. This database was first developed in 1987, and although this questionnaire has been updated throughout the years, no major revisions have occurred since Phase 4 (2000-2003). In order to compare these results to those obtained in past thesis work, [24], the same database was used: Phase 6 (2009-2011). The PRAMS database covers around 83% of all U.S. births. This database collects standardized data in survey form from volunteers across 47 states. PRAMS is administered by the Centers for Disease Control and Prevention (CDC), Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion. It is mainly focused on data before, during, and after pregnancy, and its purpose is to collect data to identify groups who might be at risk for high-risk pregnancies and to prevent these occurrences in the future [5]. Around 20% of the dataset analyzed in this research contained preterm cases.

The BORN database contains over 600,000 patient cases with over 200 general clinical features of Ontario maternal and newborn data [4]. The BORN database is a prescribed registry which has the authority to automatically collect and track health data under the Personal Health Information Protection Act [25]. The BORN database is funded by the Ontario Ministry of Health and Long-Term Care and is administered by the Children's Hospital of Eastern Ontario

(CHEO). Some of the areas of focus of the BORN database include: maternal newborn outcomes / midwifery, congenital anomalies surveillance, newborn screening, and prenatal screening [26]. This database focuses on cases solely from Ontario with data on pregnancy, birth, and childhood factors [4]. Around 8% of the dataset analyzed in this research contained preterm cases.

1.5.1. Segmenting the databases

The PRAMS and BORN database were further divided between Parous and Nulliparous cases. Parous women are women who have had previous births, whereas Nulliparous women are women who have not given birth previously. Therefore, specific features will only be applicable to Parous women (i.e. previous premature birth) and thus, will affect the performance metrics of the predictive tool. Features related to Parous and Nulliparous cases were selected with consultation from our clinical partner. This is important since certain parous features, such as previous premature birth, are known to be highly predictive of future preterm birth [17]. Although it is helpful to see how the predictive model performs for both of these case types, this predictive model should be applicable to the general population and be inclusive of all women, including those who have no prior history of preterm birth. Therefore, four datasets were modelled throughout this research: BORN_Parous, BORN_Nulliparous, PRAMS_Parous and PRAMS_Nulliparous, where the nulliparous group included both.

1.6. Thesis Objectives

The overall goal of this thesis was to develop a predictive tool which has improved sensitivity results when compared to past work done by our research group. To accurately make this comparison, the same methodology steps will be followed from Ong's work [24], except for the data preparation stage. The final goal is to be able to apply this tool prospectively at obstetrical clinics that log patient data electronically to help clinicians and provide information for families.

To fulfill this goal, three objectives must first be addressed. The first objective was to evaluate the processed data for feature reduction. There were a multitude of features in both the BORN and PRAMS database; many of these were not related to predicting preterm birth. The C5.0 Decision Tree classifier was applied to create a subset of features most important for predicting preterm birth. Utilizing this subset of features enhances the accuracy of the Artificial Neural Network during training and testing.

The second objective of this thesis is to apply data mining techniques to the BORN and PRAMS databases, with a focus on data preparation. Addressing the presence of missing values and class imbalance were the two main areas of focus in the data preparation stage. The hypothesis was that the greatest improvement in sensitivity results would be achieved by focusing on these two areas.

The third objective was to evaluate the above hypothesis; by comparing the sensitivity metrics obtained in this work with those obtained from past research (Ong [24], Yu [27] and Catley [11]). The same machine learning tools were used (DT and ANN) in past work performed [24] and the results obtained were compared to the current prediction performance, when applying new data preparation methods. In addition, the 5-by-2 cross validation technique introduced in past research [24] was applied to reduce bias and overfitting of the Artificial Neural Network Classifier. This comparison was done to observe the differences in classification results, when there is a focus on improving data quality, prior to training and testing the predictive model.

The final results should provide an assessment of the level of improvement provided by the new methodology; this approach could be followed when implementing a predictive tool at clinics collecting prenatal data, to ensure high accuracy of predicting preterm outcomes.

1.7. Thesis Outline

The outline of this thesis is as follows:

Chapter 1 outlines the motivation for this work, gives a general overview of the problem and a description on how this research work contributes to improving past research results.

Chapter 2 provides a background and detailed literature review of preterm birth. This chapter also provides a summary of past work done by researchers at the MIRG group and on data preparation methods; this section also explains, in depth, the performance metrics addressed in this research work. In addition, the machine learning classifiers and software tools used to evaluate the datasets analyzed in this work are addressed.

Chapter 3 describes the methodology of the research work: it focuses on the software tools and models used to analyze and test the clinical datasets.

Chapter 4 presents the results of the data preparation steps, model evaluation and contains a discussion on the performance metrics achieved in predicting outcomes for preterm birth, compared with previous results of other models.

Chapter 5 summarizes the final models and presents concluding remarks and the thesis contribution. In addition, this section provides suggestions for future work.

2. Chapter: Literature Review

This chapter encompasses a review of the literature based on risk factors associated with preterm birth. It includes a review of past work done by students within the MIRG lab, data preparation methods and current prediction models. This chapter describes pertinent performance metrics that will appear in later chapters and summarizes the machine learning and software tools used in this research.

2.1. Common Factors of Preterm Birth

There is often no known cause of spontaneous preterm birth but there are a multitude of factors which can lead to birth occurring at less than 37 weeks. Some of the medical factors can be preeclampsia and fetal distress, while some of the social factors can be stress and physical abuse. These factors can be grouped into three major areas leading to preterm birth: social stress and race, infection and inflammation, and genetics [28], [29]

2.1.1. Social Stress and Race

Several studies have shown a correlation between high rates of poverty and increasing rates of preterm birth [30]. Lack of access to healthcare and poor nutrition, as well as high rates of domestic abuse can be linked to poverty-stricken areas and these factors can negatively affect the health of both the baby and the mother. The rate of preterm birth amongst black women is generally higher in comparison to other races. In the United States, the rate of preterm birth in black women is twice as high as it is for white women [30]. Racial disparity in social situation and discrimination, which may lead to social stressors such as poverty and lack of access to proper healthcare, have been some of the reasons cited for this gap.

2.1.2. Infection and Inflammation

Another key factor linked to high rates of preterm birth is intrauterine infection and inflammation. Bacterial infection can be widespread and can be found between the maternal tissues and fetal membranes, within the fetal membranes, within the placenta, within the amniotic fluid, within the umbilical cord, and within the fetus [30]. Bacterial infection often results in inflammation of the tissues and this response can trigger a premature labour and subsequent birth.

2.1.3. Genetics

There is some evidence that maternal genes have a large influence on the risk of preterm birth [30]. Therefore, one could review the family history of the mother to determine if relatives have had preterm births and this might be indicative of a predisposition to preterm birth. In addition, women who have had previous preterm births are at a higher risk for subsequent births to also occur prematurely [17].

2.2.Cost of Preterm Birth

The burden of premature births on health-care costs is significant. Patients born prematurely are hospitalized for longer, need to be monitored more regularly, and use more hospital equipment than full-term birth patients, as they are susceptible to a host of diseases and illnesses. Some of the medical devices often used patients born prematurely are incubators, multiple infusion pumps, invasive and non-invasive monitors, and ventilators. After discharge from hospital, premature infants are more likely to be re-hospitalized than full-term babies. It is estimated in Canada that the average hospital care cost for a preterm baby is nine times greater than a full-term baby [31]. For full-term babies, it is estimated that they will remain in the hospital for around two days, whereas with preterm babies, the hospital stay may be as long as 104 days [31].

Due to these factors, it is estimated that the hospital care cost of a preterm baby in Canada may extend upwards to $117,000 [31].

2.3. Health of Preterm Infants

Preterm delivery can result in the infant having several long-lasting disabilities. Premature infants have underdeveloped organs, specifically the lungs and heart. This can lead to severe neurological and cardiovascular problems. For instance, some infants can have respiratory distress, apnea and feeding problems; these illnesses all result in a longer hospitalization for the patient. One study showed that children at age eight who were born prematurely had more behavioural problems than their peers born full term [32]. Premature birth will likely impact the individual's life in the long term, with chronic lung disease and intellectual and developmental handicaps occurring commonly in those patients born most prematurely.

2.4. Current Prediction Models

2.4.1. Cervical Length

As previously stated, there is not one identifiable factor known to predict preterm birth; however, a correlation between the rate of shortening of the cervix and the prevalence of preterm birth has been observed. For instance, in one study, [33] researchers focused on women whose cervixes were shortening between 16-20 and 21-25 weeks and regularly observed the progression of their pregnancy. They found that if the cervical length was stable for periods of time and then would suddenly and rapidly decrease, this would often result in a preterm birth. Although this is an interesting finding, in practice it is difficult to observe patients sufficiently regularly to detect these changes and the detection methods are invasive and so a more realistic prediction model would be helpful in clinical work.

2.4.2. Uterine Electromyography

Uterine Electromyography (EMG) is the practice of monitoring uterine contractility using electrodes placed on the uterus and can detect when there is increased contractility signaling the possible onset of preterm birth [34] With this method, the patient has to remain as still as possible when collecting these signals; if not, this can result in noisy signals which have to be filtered. In addition, the accuracy of this prediction model tends to be most accurate within a short window of labour (24 hrs to 4 days), similar to the fetal fibronectin test [34]. However, the focus of this thesis is to detect a preterm birth accurately, many weeks prior to labour, so that preventative care can be administered.

2.4.3. Fetal Fibronectin Test

The fetal fibronectin test has become the gold standard for predicting preterm birth. However, this test is expensive, invasive, and it is best designed as a short-term marker for preterm birth, as the sensitivity decreases from 71%, 67% and 59% within 7,14 and 21 days of delivery [35]. It is typically only measured after the membranes lining the uterus have ruptured, which is often the sign of impending preterm labour. Fetal fibronectin is a protein produced by fetal cells which forms a major portion of the maternal-fetal extracellular matrix [35]. Cervicovaginal leakage of this protein in the late second and early third trimester has been an indicator in many cases of spontaneous preterm birth [35]. The goal of this work, however, is to develop a tool that can be applied non-invasively and throughout the early stages of pregnancy, before any signs of preterm labour develop.

2.4.4. Physician-Parent Decision Support (PPADS)

The PPADS tool was developed in the MIRG lab at Carleton University and is a tool which provides shared decision-making between physicians and parents, concerning infants in the NICU [36]. The PPADS tool consists of two platforms: a clinician and a parent interface. The parent interface provides information about the infant with mortality risk estimations and provides a decision support module, allowing parents to communicate and understand the options available to them. The clinician interface contains the list of all patients, admission files and various medical details including outcome predictions. The PPADS system is currently being remodeled and a dictionary of medical terms will also help to enhance parents understanding of their child's condition.

2.4.5. Ontario Perinatal Record

Since 1997, The Ontario Antenatal Record consisted of a form which collected pregnancy data, and was administered by maternal care providers in Ontario. The Ontario Medical Association (OMA) had been the primary driver of distributing and updating this form. Recently a new partnership has arisen between the Provincial Council for Maternal Child Health (PCMCH), The Better Outcomes Registry & Network (BORN) Ontario, the OMA and the Association of Ontario Midwives (AOM), to create an expanded scope of these forms called the Ontario Perinatal Record [37]. The questions within this form pertain to pregnancy, birth, and the early newborn period [37]. There are clinics in Ontario where this information is being entered electronically and one future method of monitoring patients for early risk of preterm birth would be to embed the tool developed in this research to be used in conjunction with the Ontario Perinatal Record to

automatically screen the data as it is being collected and flag patients who are deemed to be at risk of preterm birth.

2.4.6. Predictive Tools

A preterm risk scoring tool is a means of risk assessment which contains many major or minor factors (previous preterm delivery, smoking/alcohol intake during pregnancy, etc...) and it estimates the likelihood of the outcome of a preterm birth [38]. Preterm risk scoring, and screening tools have been administered since the 1980s; however, the accuracy of these tests remains quite low, at around 17-38% [38]. This can lead to a waste of hospital resources and therefore, a more effective and accurate system is needed that balances both high sensitivity and specificity metrics. One of the problems with current risk scoring tools is that they are often limited in their capabilities. This is related to the fact that currently there is no specific cause of spontaneous premature birth—just a multitude of factors which can contribute to a premature birth occurring. The advantage of using machine learning tools over risk scoring methods is the ability to easily analyze hundreds of possible preterm birth factors. The benefit of risk scoring systems is that they do identify the complex social and environmental factors which surround the risks of preterm births

2.5.Summary of Previous Work

Catley

The objective of Catley's thesis work was to develop an integrated hybrid classifier which combined ANNs (artificial neural networks) and MLP (multilayer perceptron)-ANNs with risk stratification. She also used case-based reasoning and a DT (decision tree) voting algorithm to predict preterm birth using an older version of the PRAMS database and the Perinatal Partnership Program of Eastern and Southerneastern Ontario (PPPESO) database (1999-2001).

The results from this classifier yielded a sensitivity of 65% and a specificity of 84% and was validated with 9701 new patient cases. The data preparation methods used in this thesis work were to remove features with greater than 20% missing values and the k-NN (k-nearest neighbor) CBR (case-based reasoning) algorithm, for imputing missing values [39].

Yu

The objective of Yu's thesis was to combine an Artificial Neural Network and Decision Tree classifier: C4.5 DT Classifier [40] to output an integrated classifier to reduce the number of features and to increase the overall accuracy of the classifier. The model was validated using the PRAMS database and this integrated classifier could predict mortality rates with a sensitivity of 65% and a specificity of 84%. The data preparation methods used in this thesis work were similar to Catley's: deletion of features with greater than 50% missing values, and the use of the k-NN CBR for imputation of missing values [27].

Ong

The objective of Ong's thesis was to improve the integrated classifier and to apply this classifier to two recently updated databases, (PRAMS and BORN) to predict mortality rates. This thesis also uses 5-by-2 cross validation to both ensure the model is trained with sufficient data and reduce overfitting. In addition, many more features were analyzed than in Yu's work, with factors obtained from four different types of cases: Parous, Nulliparous, Parous without Obvious clinical features, and Nulliparous without Obvious clinical features. The best performance metrics achieved was the PRAMS Parous dataset: 50% for sensitivity and 92% for specificity when analyzing around 53 clinical features. The data preparation methods used in this thesis work were to remove outliers, deletion of features with greater than 50% missing values, deletion

of cases with no outcome feature, and the use of the k-NN CBR as an imputation method for missing values [24].

Other Research

Research concerning predictive tools which use obstetrical data/devices and machine learning algorithms have been investigated. In work done by [41], this work consists of using uterine EMG data and artificial neural networks to classify preterm or term cases. The results were promising, the ANN was able to classify preterm cases with an accuracy of 92% and was able to classify term cases with an accuracy of 79%. Also, in [42], the focus of this research was to document factors of importance by studying high-risk women from their first antenatal visit straight through to delivery. Researchers used logistic regression and artificial neural networks to identify significant risk factors (i.e. biochemical markers) which are associated with preterm birth. Finally, [43], also made use of the C5.0 DT classifier and ANN as machine learning tools, yet, the focus was on determining the top risk factors of preterm birth, in comparison to improving the sensitivity in this research. Factors such as maternal age, multiple births and maternal hypertension were just some of the factors which were identified to be of importance in predicting preterm birth. Predictive methods using machine learning algorithms are being studied extensively within the field of obstetrics, in search of faster, more accurate methods of predicting preterm birth.

2.6. Review of Data Preparation

There were two main areas to address in the data preparation stage; the presence of missing values and class imbalance in BORN and PRAMS.

2.6.1. Missing Values

There are three general categories of missing values [44]:

1) Missing Completely at Random (MCAR)

2) Missing at Random (MAR)

3) Not Missing at Random (NMAR)

MCAR refers to random experimental error which affects the presence of an attribute; MAR refers to features which are not missing at random, but whose value depends on other measured features; NMAR refers to features not missing at random; the probability of this missing attribute depends on unavailable features. It is easier to impute missing values for MCAR and MAR variables, than NMAR [45].

When the probability that the data is missing, is the same for all features in the dataset (e.g. no blood pressure equipment to measure heart rate), this would fall under the category of MCAR. When the probability that the data that is missing is dependent on observed data (e.g. study on blood pressure, data on young people are less likely to be recorded, in comparison to older individuals because they do not attend clinics as often); this would fall under the category of MAR. Finally, when the probability that the data that is missing is dependent on data that has not been observed (e.g. individuals with lower incomes are often less likely to fill out information related to income), this represents NMAR [46]. As detailed in these examples, first-hand knowledge of the observed data is a key to making assumptions about features and which category the data falls under. The PRAMS dataset consists of survey data and BORN consists of automatically obtained data. Thus, there is little room for researchers to make assumptions because this data is obtained from external sources.

2.6.2. Discussion of Alternative Imputation Methods

There are several methods for imputing missing values. Some of these methods have been analyzed below, to determine the best method of addressing missing values within the BORN and PRAMS datasets.

2.6.3. Simple Imputation Methods

There are simple imputation methods such as calculating the mean or mode of the feature to fill in missing values. However, calculating the mean or mode does not translate well for categorical features and ignores correlations between features within the clinical datasets [47].

2.6.4. k-NN Algorithm

In previous work [24], a k-NN algorithm was used for imputing missing values through a CBR tool developed in Microsoft Access. The k-NN algorithm makes two assumptions which make this algorithm ineffective for this research when compared to other imputation methods. The first assumption is that the data in the feature space are continuous [48]. Both the BORN and PRAMS datasets contain mixed type features (both categorical and nominal). Usually Euclidean distance is used as the distance function to measure differences between continuous features [48]. The second assumption is that the user must choose the k-value; this is usually done through cross validation [47]. The "k" value represents the number of neighbours which influence the classification. Difficulties related to these two assumptions were crucial in the decision to adopt another imputation method in this current research. There is a delicate balance between increasing the k-value, improving the accuracy and increasing the computational time. This is exemplified with Ong [24], where it was reported that it took up to three days to analyze these

clinical datasets using this algorithm and the CBR tool. In addition, there are software programs (R) which drastically reduce the processing time from three days to hours.

2.6.5. mice Algorithm

The mice (Multivariate Imputation via Chained Equations) algorithm, as the name suggests, creates multiple imputations to reduce bias of results [49]. This algorithm was developed by Stef van Buuren and is a package in R. In the first step of the mice process, each missing value is temporarily set to the mean value within that feature. Then using one of the regression methods from the mice function (see Figure 2.1), which matches the data type of the feature, a missing value is obtained. This process is repeated as specified by the user; usually this cycle is repeated ten times [50]. The mice algorithm uses linear regression to predict nominal missing values and logistic regression for categorical missing values. The methods for the mice function are displayed below.

Method	Description	Scale type	Default
`pmm`	Predictive mean matching	numeric	Y
`norm`	Bayesian linear regression	numeric	
`norm.nob`	Linear regression, non-Bayesian	numeric	
`mean`	Unconditional mean imputation	numeric	
`2L.norm`	Two-level linear model	numeric	
`logreg`	Logistic regression	factor, 2 levels	Y
`polyreg`	Multinomial logit model	factor, >2 levels	Y
`polr`	Ordered logit model	ordered, >2 levels	Y
`lda`	Linear discriminant analysis	factor	
`sample`	Random sample from the observed data	any	

Figure 2.1. Regression methods in the mice algorithm to impute missing values [49]

2.6.6. Chosen Method: missForest Algorithm

The missForest algorithm is a function which uses random forest classifiers to train each feature, and then this model is used to make predictions about missing values [48]. This algorithm was developed by Daniel Stekhoven and is a package in R. This function also provides an imputation error estimate for both the categorical and nominal data. Some papers show that missForest outperforms mice with a lower imputation error [47], [48]. In addition, with the mice algorithm, even though this algorithm has the capability to handle multiple types of data, one must make this explicit, coding in R. For instance, if one of the features in the dataset is numeric, then this had to be defined in the code as 'pmm' (predictive mean matching when using the mice algorithm). Similarly, when one of the features had two factors (i.e. "Yes" or "No") with two levels, this was defined to be 'logreg' for logistic regression, and if another feature had more than two levels, then this would be defined as 'polyreg' or multinomial logistic regression model. With many mixed types in the dataset, this process can become tedious. Similarly, to the k-NN algorithm, the number of imputed datasets with the mice model is controlled by the user.

Although the value of 10 seems to be the most widely chosen option, research has seen improvements in accuracy when this value is chosen to be anywhere up to 40 [50]. Therefore, again a trade-off between accuracy and computation time exists. The computation time using missForest in this research work was significantly faster than using mice, when the number of imputed datasets was chosen to be 10. For instance, using missForest, the processing time took around 16 hours, while with mice repeating the process 10 times took around four days to complete. Also, as the mice algorithm is a multiple imputation method, this algorithm operates under the assumption of MAR (missing at random) [51]. However, there is a risk of biasing the results if this assumption is made without strong justification [51]. Since, missForest is a non-

parametric algorithm, this removes the researcher from having to make incorrect assumptions about missing values within features.

2.6.7. Class Imbalance

Most medical data contains an imbalance of classes, with the disease case usually being the rare occurrence in a dataset [52]. This is exemplified in both the PRAMS and BORN datasets, where the preterm cases represent around 20% and 8% respectively. This creates imbalanced datasets which affects the classification accuracy during training and testing [53], [54].

2.6.8. Discussion of Alternative Class Imbalance Methods

If the dataset is not balanced during training, the classifier output could be biased, and the classifier could misclassify a preterm birth label as a term label. In this case the classifier views the small proportion of preterm labels as noise or outliers, in comparison to the larger set of term labels. Thus, the specificity metric of the classifier will be very high while the sensitivity will be low. It is necessary to balance the class labels so that the ANN classifier will be less biased [55]. In this research, it appears to be a more serious misclassification to falsely predict a preterm label as a term label, than a term label as a preterm label.

2.6.9. Get more training cases

Obtaining more training cases can be expensive and may be unavailable; it may not be possible for researchers to get more cases. In our research, related to time restrictions (i.e. preparing a dataset from BORN could take on average 6-8 months), it simply was not feasible or cost effective to request more preterm cases from the BORN and PRAMS datasets. It is always quite complicated to obtain ethics clearance to acquire new data.

2.6.10. Oversampling the minority class

Oversampling the minority class would entail replicating the preterm cases. The disadvantage of this method lies in possible overfitting of the minority class, as there are many more samples created from replicating the minority cases [56], [57]. Also, with over 600,000 cases in the BORN dataset and over 100,000 cases in the PRAMS dataset, oversampling would significantly increase the size of these datasets; leading to increased computational time for training and testing the Artificial Neural Network classifier.

2.6.11. Chosen Method: Undersampling the majority class

Several papers have reported the benefit of undersampling over oversampling when dealing with class imbalances. Oversampling may result in over-fitting of the classifier and will result in longer training times due to the increase in the sample size [56]. Although the disadvantage with undersampling is the loss of "valuable" information, the focus of this research is on accurately predicting preterm cases. The most "valuable" information lies in the preterm cases. Reducing the number of term cases, greatly improved computational time and sensitivity results during the training and testing of the neural network classifier.

2.7. Performance Metrics

2.7.1. Confusion Matrix (Contingency Table)

The purpose of a confusion matrix is to showcase the predictions from a classification model versus the accurate predictions, to determine the efficiency of the model in predicting an outcome [58]. For instance, in Table 2.1., the positive column displays both the true predictions from the model output and the number of predictions the model "classified" as false predictions, but which were true.

Table 2.1 2-by-2 Confusion Matrix

	Actual Value		
Predicted Value		Positive	Negative
	Positive	True Positive (TP)	False Positive (FP)
	Negative	False Negative (FN)	True Negative (TN)

2.7.2. Correct Classification Rate (CCR)

This metric is a measure of the accuracy of the model in being able to predict cases [59].

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN}$$

2.7.3. Misclassification Rate

This metric is a measure of how often the model makes an incorrect prediction [59].

$$Missclassification\ Rate = \frac{FP + FN}{TP + TN + FP + FN}$$

2.7.4. Sensitivity

Sensitivity (True Positive Rate) is a specific parameter focusing on the ability of the classifier to accurately classify a case which is defined as positive [58]. For instance, a positive case can be defined as a patient having a preterm birth (or a specific disease). Therefore, if the sensitivity of your test is 100%, this means the test will correctly label all patients who have preterm birth as preterm births.

$$Sensitivity = TPR = \frac{TP}{TP + FN}$$

2.7.5. Specificity

Specificity is a specific parameter focusing on the ability of the classifier to accurately classify a case which is defined as negative [58]. Continuing with the same above example, if the negative case is defined as the patient having a full-term outcome, a specificity of 100% means that the test would correctly label all patients who have births to term as full-term outcomes.

$$Specificity = TNR = \frac{TN}{TN + FP} = 1 - False\ Positive\ Rate\ (FPR)$$

2.7.6. F1-Score

This score functions as a weighted average of the precision and recall. The closer the classifier's F1-score is to 1, the higher the precision and recall values will be [60].

$$F1 = \frac{2TP}{2TP + FP + FN}$$

2.7.7. Prevalence

Prevalence is a measure of the prior probability of the individual having the disease before the model is tested given the population size [61]. It is an important measure for the MIRG group as it ensures clinical relevance and acts as a threshold. In the context of this research, prevalence would relate to the proportion of the population who have had a preterm birth. In Ontario, the prevalence of preterm birth is around 7.9% [16]. As a result, during the final testing stage, the test sets evaluated by the ANN will use the prevalence in the population.

2.7.8. Positive Predictive Value & Negative Predictive Value

The positive predictive measure is defined by the probability of truly having the disease, given a positive outcome from the test, whereas the negative predictive value is the probability of not having the disease given a negative outcome [58]. There is a direct correlation to the PPV and the prevalence, where if the prevalence is low the PPV will also decrease.

$$PPV = \frac{TP}{TP + FP} \times 100$$

$$PPV = \frac{Sensitivity \times Prevalence}{Sensitivity \times Prevalence + (1 - Specificity) \times (1 - Prevalence)} \times 100$$

$$NPV = \frac{TN}{TN + FN} \times 100$$

$$NPV = \frac{Specificity \times (1 - Prevalence)}{Specificity \times (1 - Prevalence) + (1 - Sensitivity) \times Prevalence} \times 100$$

2.7.9. Receiver Operating Characteristic (ROC) Curve

The ROC is a curve displaying the performance of the ANN classifier at all classification thresholds, the x-axis is the sensitivity (true positive rate) and the y-axis is derived from 1-specificity (false negative rate). This curve also displays the trade-off between sensitivity and specificity. In this research the purpose is to obtain classifier results which optimize sensitivity but also maintains a relatively high specificity. If the curve rises quickly in the beginning, this might indicate better classifier performance when comparing different ROC curves [58]. Figure 2.2. highlights the features of importance in the ROC curve [24].

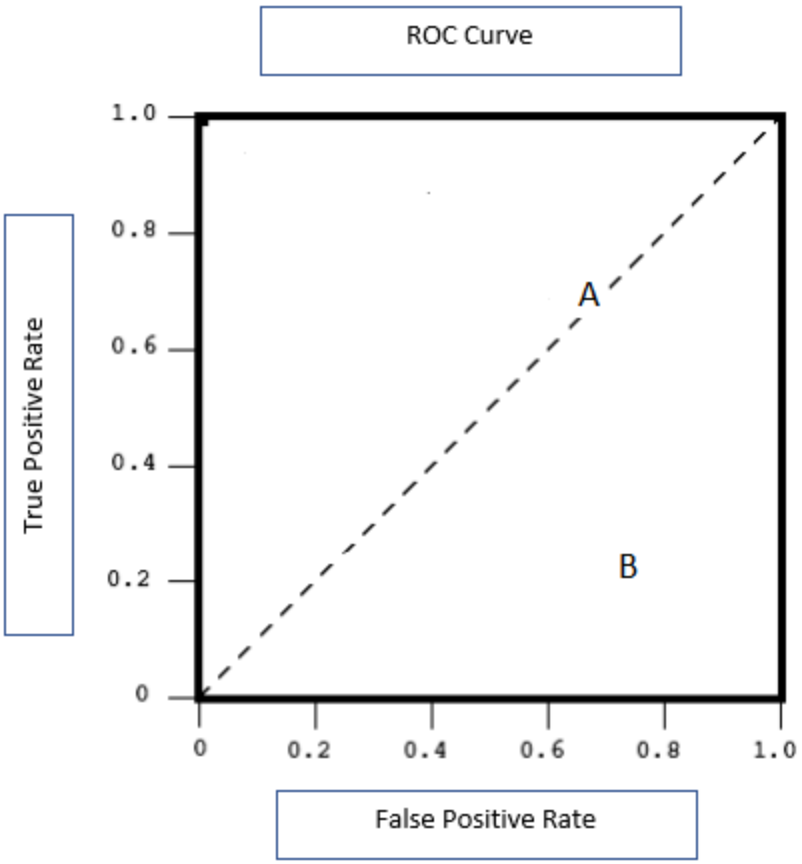


Figure 2.2. ROC curve and the different points of significance

- At coordinate (0,0) there is no positive classification given and therefore no false positive classification exists. At point (1,1), the classifier assigns a positive class label to all points hence it is where the false positive rate is at its max. At point (0,1) the classifier has 100% sensitivity and specificity and represents perfect ability to discriminate between preterm and term cases
- A diagonal line (A) indicates random guessing. Points on this line indicate that TPR and FPR are equal thus classifier performance is random and does not contain useful information.
- Point B, falling below the A line is worse than random guessing. May indicate that useful information is contained in the classifier however the application is incorrect.

2.7.10. Area Under the Curve (AUC)

The AUC is a measure of how accurate the classifiers predictions are. An AUC value of 1 represents 100% accuracy in predicting preterm births, while an AUC accuracy of 0 represents 0% accuracy in predicting preterm births. An AUC value should strive to be above 0.5, as 0.5 represents a classifier which is as good as random guessing. The effectiveness of this value is summarized in Table 2.2. [62].

Table 2.2 AUC Index and its Effectiveness labels

Min	Max	Effectiveness
	≤ 0.5	No discrimination
0.5	< 0.7	Poor discrimination
0.7	0.8	Acceptable
0.8	0.9	Excellent
0.9	1.0	Outstanding

2.7.11. Mathews Correlation Coefficient

The Mathews Correlation Coefficient (MCC): is a correlation coefficient between the observed and predicted classifications. This metric varies between -1 and 1, -1 indicates a completely wrong binary classifier, 0 represents an uncorrelated classifier (as good as random guessing) and 1 indicates a completely correct binary classifier [63].

$$MCC = \frac{(TP \times TN) - (FP \times FN)}{\sqrt{(TP + FP)(TP + FN)(TN + FP)(TN + FN)}}$$

2.7.12. Normalization

Normalization was an important preprocessing step before evaluating the data with the Artificial Neural Network, this was done using the modified Z-score transformation. Normalizing refers to scaling the data to fall within a certain range. The ANN deals with nominal data and the BORN and PRAMS data contains categorical and nominal data. Therefore, it was important to normalize the dataset so that all the features were in the same range and no specific feature was given more weight than others during the training stage. There are several methods to normalizing the data. Options include centering the data to have a mean of 0 or scaling the data by the standard deviation [64]. Past work has shown that the neural network works best when normalized between the range of [-1,1], [13]. The normalization process will be expanded on in greater detail in Chapter 3.

2.8. Pattern Classification Methods

Pattern classification methods have been used with fields such as, medical informatics, to classify and categorize large amounts of medical data and output clinical outcomes when faced with medical problems. The two types of pattern classification tools used within this thesis are: Decision Tree (DT) and Artificial Neural Network (ANN) classifiers. Specifically, a hybrid classifier which uses both elements from the DT (feature reduction) and the ANN classifier (model evaluation) are used to classify the preterm and term cases.

2.8.1. Supervised Learning

Supervised learning is a type of machine learning process which contains labels in the output variable and this differentiates this type of learning from unsupervised learning. Furthermore, supervised learning can be classified into two categories: regression and classification [65], [66].

A regression problem is described as having a numerical real value label such as “weight” and a classification problem is described as having a categorical output label such as “preterm”. This work deals with supervised learning, as the main objective is to determine an accurate preterm birth outcome label, using an Artificial Neural Network classifier.

2.8.2. Unsupervised Learning

Conversely, unsupervised learning is a type of machine learning process which contains no output labels. Unsupervised learning can also be classified into two categories: clustering and associations. As the name suggests clustering refers to understanding how groups (clusters) respond to certain features in a given dataset. Association refers to what rules or relations one can make based on similarities between groups [65], [67].

2.8.3. Semi-supervised Learning

Semi-supervised learning takes aspects from both supervised and unsupervised learning. Semi-supervised learning contains labeled and mostly unlabeled data. Given this mix of labels, one could approach the problem with both an unsupervised or supervised approach. For instance, if one wanted to learn about patterns and structure of the data, an unsupervised learning algorithm could be one option [68]. However, in this work, the method used on the data would be a supervised learning approach for the dataset, as the objective is to accurately predict the unlabeled data with the labeled data provided [69].

2.9.Feature Reduction

Data reduction is a large section of data preprocessing [70]. The “curse of dimensionality” refers to the situation where it is often beneficial to limit the number of features to maintain classifier performance [71], [70]. A decrease in classifier performance might be related to overfitting,

when the classifier is provided with too many features. When the classifier sees new data that it previously has not been trained on, the classifier performs poorly. Thus, appropriate feature selection (FS) is important to maintaining a high accuracy for the ANN, (especially since this classifier has a non-linear decision boundary prone to overfitting, in comparison to other classifiers [72]). Currently there are hundreds of features in both the BORN and PRAMS datasets and, by pruning these features down to an optimal subset, one can obtain improved classifier performance; it makes sense not to use all the clinical features provided during training.

There are many FS (feature selection) methods to draw from, and these are the three main categories [10]:

1) Filter FS methods
2) Wrapper FS methods
3) Embedded FS methods.

In Method 1, the features selected are independent of the classifier; the features are ranked based on a specific statistical measure (i.e. entropy) and chosen based on rank; in Method 2 the features are dependent on the classifier; a subset of feature is chosen and evaluated on the classifier, and the subset of features with the best classifier performance is chosen. The final method is akin to Method 2; however, these methods are much faster than the wrapper methods. This feature selection method occurs during the learning process.

2.10. Machine Learning Tools

2.10.1. Decision Tree Classifier

Decision Tree Classifiers are supervised classification methods where decision-based rules, determined by the features, are input into the classifier [73]. There are a variety of DT classifiers: ID3, C4.5 and C5.0 [74]. Figure 2.3 depicts the framework of a decision tree classifier. A DT classifier consists of nodes, branches and leaves, where the nodes represent the features, the branches represent the decision rule associated with the node and the leaf represents the terminal outcome (preterm or term in this case). To begin the classification, a statistical measure (i.e. entropy) is calculated for each feature and the feature with the highest value is chosen to be the root node; this process is repeated until the outcome is achieved [72] .

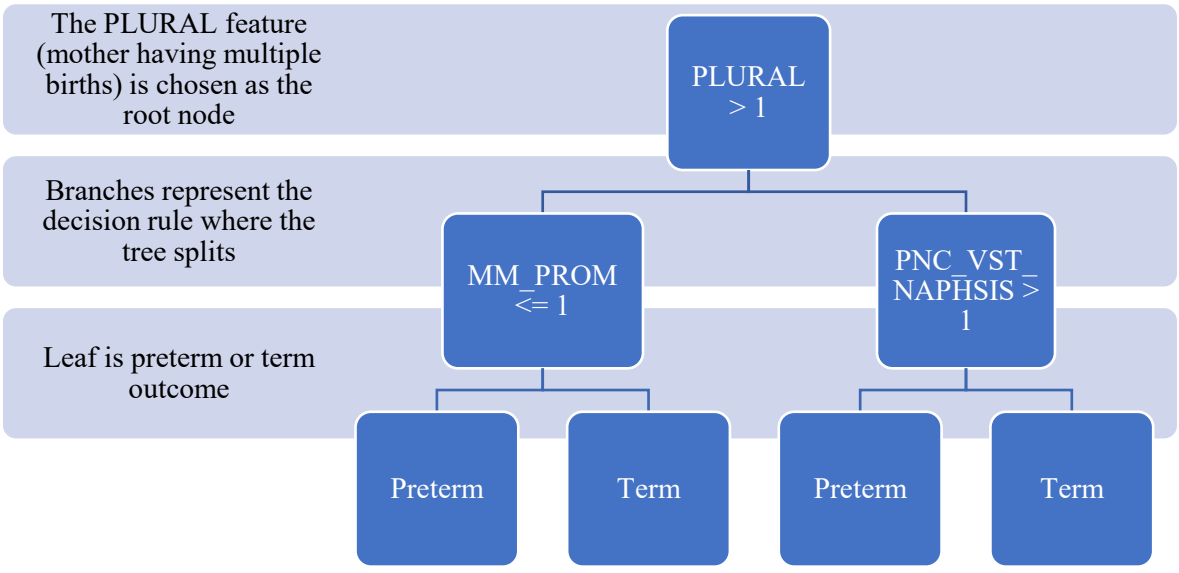


Figure 2.3 Depiction of the Decision Tree Classifier Framework [75]

Some advantages to using DT classifiers include:

- The model is intuitive
- Data preprocessing is minimal (Decision Tree C5.0 can handle missing values)

Some disadvantages to using DT classifiers include:

- Risk of overfitting results
- In cases where the dataset has class imbalance, a biased tree can be produced

The disadvantages to using DT classifiers have been dealt with throughout this thesis work by firstly using cross validation, and secondly, by separating the validation set from the original dataset. This was done when testing the Artificial Neural Network (ANN) classifier, to reduce the risk of overfitting results. The second disadvantage of creating a biased tree was reduced by under-sampling the majority class of term cases by using the undersampling package in R [76]; these details will be expanded on later in the thesis.

2.10.2. Random Forest Classifier

The random forest classifiers can be described as a randomized ensemble of decision trees, as observed in Figure 2.4. The random forest classifier is a type of supervised learning algorithm which differs from decision tree classifiers. The DT classifier splits the features based on the most important statistical measure (i.e. entropy) in the feature subset; the random forest classifier splits features based on the most important statistical measure, derived from a random subset of features; this adds randomness to the model and reduces the correlation between trees. This creates a separate classification outcome for each tree, which is then aggregated, and a final vote is done [48], [77], [78].

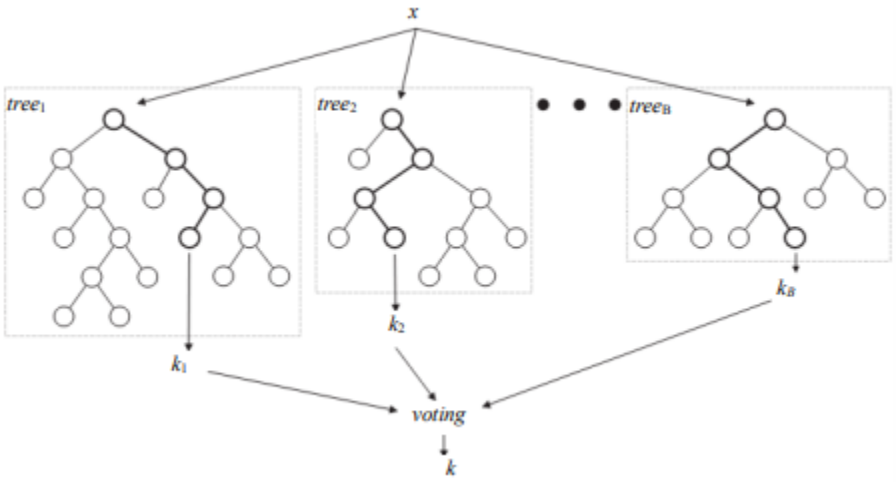


Figure 2.4. Depiction of the Random Forest Classifier Framework [79]

2.10.3. Artificial Neural Networks

Artificial Neural Networks were modeled to mimic processes within the brain. Artificial Neural Networks consist of mathematical algorithms which have a similar basic framework (see Figure 2.5): inputs are multiplied by a weight (this is assigned based on relative importance in comparison to other inputs) in the Input layer and passes into an activation function in the Hidden layer which produces an output (preterm or term) in the Output layer. Then, Input 1 is multiplied by the weight (-0.14) along with the other inputs and weights, is summed and the activation function is present in the Hidden layer, resulting in an Output value of 1. There are several types of ANNs; some of the formulations include multilayer perceptron (MLP) and Radial Basis Function Networks (RBFNs) [70]. The specific activation function used in this research work was a sigmoid symmetric function (also known as the tanh function) which gives an output between [-1, 1] (see Figure 2.5), this is one of the most widely used functions for layered feed-forward networks [7], [80]. Other non-linear functions are the ReLU (Rectified Linear Unit) activation function which thresholds the output at 0 and replaces negative values

with 0. The output from the classifier is compared to known cases and adjusted by repeating this entire process again until a minimum error rate is achieved [70].

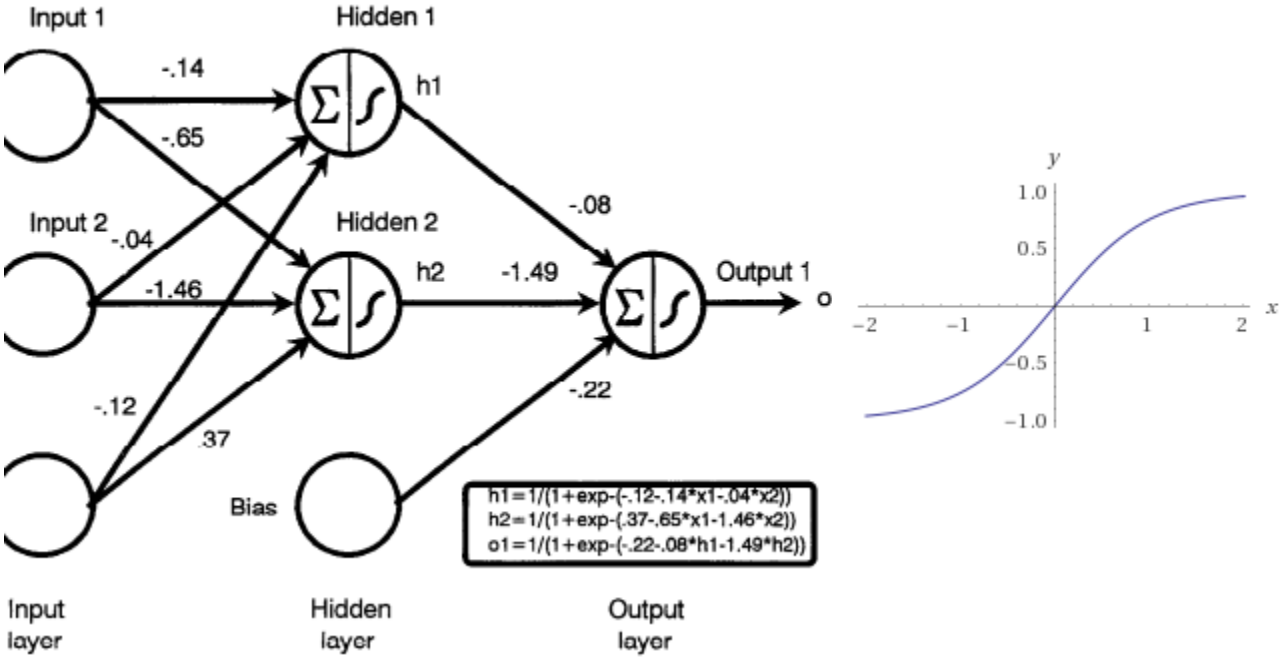


Figure 2.5. Depiction of the Activation Function and Artificial Neural Network Framework [81]

Some advantages of using ANN classifiers include:

- Performs well with regards to non-linear models
- Ability to learn models in real time

Some disadvantages of using ANN classifiers include:

- Sensitive to scaling features
- Does not do well with missing values

The disadvantages of using ANN classifiers have been addressed throughout this thesis work by normalizing the dataset before applying the ANN classifier and using the missForest package in R [48], to deal with missing values in both the BORN and PRAMS datasets.

2.11. Software Tools Used in This Research

2.11.1. R

R (1993) is a statistical programming language which was created by Ross Ihaka and Robert Gentleman at the University of Auckland, New Zealand. R is a versatile program which is open source and can be integrated into several different platforms. R also contains several packages produced by academics and data scientists, some of which have been used for data cleaning in this research work to deal with missing values and class imbalance. Packages (missForest and ubUnder) were tested to determine which one offered the best fit with the clinical data provided [48], [76].

2.11.2. Tableau

Tableau software (2003) is a tool developed by Pat Hanrahan, Christian Chabot and Chris Stolte, which allows for data visualization [82]. This program was instrumental in transforming the raw data into informative graphics. The benefit of this approach was to be able to see which of the over 100 clinical features present in these two clinical datasets, (BORN and PRAMS), were strongly correlated with a preterm or a term outcome, so that further statistical analysis could be carried out in R. Tableau offers many different charts and diagrams such as: pie charts, geographical maps and bar charts. The ability in Tableau to easily display plots and graphs was important in communicating project goals.

2.11.3. Cygwin Terminal

The Cygwin terminal was used in this research to run several Bourne-Again-Shell (BASH) scripts for the C5.0 DT classifier and ANN classifier. This software provides a Unix-like environment and is an open source platform [83].

2.11.4. See5/C5.0 Decision Tree Classifier

See5/C5.0 is a data mining tool developed by © Rulequest Research 1997 [84]. The C5.0 decision tree classifier is an updated version of the popular C4.5 decision tree classifier [74]. Some of the improvements in the latest version are the ability to deal with noisy or missing data, boosting (that is using multiple decision tree classifiers for improved accuracy) and the ability to predict which features are important. The last point was of great significance to this research work. There are over 200 features in the PRAMS dataset and over 300 features in the BORN dataset; these datasets are focused primarily on maternal health factors; thus, there are many factors which are not directly related to predicting premature birth. Obtaining a set of features which contains only those features that are relevant to preterm birth reduces computational time, noise, the "curse of dimensionality" and subsequently increases the accuracy of the ANN. Decision trees are often used for feature selection because they display a good balance of high computational speed and high performance of the selected feature subset [10]. Removing irrelevant features will improve the accuracy and speed of predicting premature births when this adjusted data is inputted into the Artificial Neural Network (ANN) model. The C5.0 algorithm can handle missing values and displays the percentage attribute usage. This tells the user how important some features are in predicting a preterm birth outcome. In addition, this algorithm incorporates adaptive boosting. In this research, ten DT classifiers were generated instead of one, and each classifier voted for the predicted class (preterm or term); the votes were counted to determine the final class. This feature incorporated into the C5.0 algorithm, reduces the error rate significantly, instead of relying on one single classifier.

2.11.5. Fast Artificial Neural Network Library

In previous work done by Catley [39] and Yu [27] the ANN was created using MATLAB software; however, MATLAB's Neural Network Toolbox is not open source software and there was difficulty in integrating it manually into the real time PPADS system. Previous work [85] focused on implementing a multilayer feed-forward-backpropagation ANN. Previous students have improved the ANN architecture through the years. The ANN-RFW (Artificial Neural Network Research Framework) developed by Rybchynski [86] was intended to improve automation and increase the prediction ability of ANNs. The problem with the use of this ANN is that it is difficult to integrate this classifier into the clinical environment; we wanted to use an ANN classifier which could quickly analyze large sets of clinical data.

The solution was to use the FANN (Fast Artificial Neural Network) Library to develop an ANN for classification purposes [7]. The advantage of using this library is that it has access to feed-forward ANNs and the library is based on the C language which makes the FANN library easy to integrate with many different software environments. Also, the FANN library allows the user to easily manipulate the same ANN parameters used in past work [86]. In addition, the FANN library has access to feed-forward networks and these networks have superior computation abilities—which is critical for processing large amounts of medical data. Neural networks are also beneficial in identifying patterns and in identifying which trends deviate from these patterns. Articles have reported the benefits of using neural networks focused on classification problems and more specifically in the medical industry, such as with medical imaging [87], [88].
The ANN Builder can be run in several different modes: FAST, MEDIUM and SLOW. The FAST mode analyzes around 0.5% of all neural network combinations, MEDIUM mode

analyzes around 7% of all options, and SLOW runs through all possible combinations. This feed-forward artificial neural network is also multilayer, indicating an initial input phase, a defined number of hidden layers, and ending with an output layer. There are three phases for these neural networks (NN): a training, testing, and validation phase. The training and testing phases consist of feeding the NN both preterm and term cases, so it can learn to differentiate between these two classifications. The validation phase consists of inputting the NN cases that it has not previously seen (unlabeled data) and it outputs final classification labels as either preterm or term. There is user flexibility involved with this software; factors such as the learning rate, the activation function, the steepness value of the activation function and the values of the initial weight of the neural network can be manipulated by the user.

15 network parameters available through the FANN library [7] are listed below:

1. Connection rate
2. Number of hidden layers
3. Number of hidden nodes: Defines the number of nodes in each hidden layer
4. Connection weights: Two options available- randomly assign values to weights or initialize weights (Widrow-Nguyen algorithm)
5. Activation functions: There are six activation functions available- Sigmoid symmetric, Gaussian symmetric, Elliot symmetric, Linear piece symmetric, Sine symmetric, Cosine symmetric; all these functions output a value between -1 to 1.
6. Activation steepness: Determines the speed at which the activation function goes from the minimum to the maximum.
7. Training algorithms: Four training algorithms available- Incremental training, Batch training, Quickprop training, Rprop training

8. Learning rate: Determines the speed at which the network attains a minimum in the criterion function.
9. Training error function: Two error functions are available: A standard linear function or a hyperbolic tangent error function.
10. Incremental training momentum: This parameter speeds up the training y adding a proportion of the previous weight-change value to the new value
11. Quickprop training weight decay factor: Determines how much the weights need to be penalized to make sure they do not become too high during training.
12. Quickprop training maximum growth factor: Restricts the size of weights' growth
13. Rprop intial step-size: Determines the initial step-size for weights
14. Rprop step-increase: Determines how much the step size can increase during training.
15. Rprop step-decrease: Determines how much the step size can decrease during training.

3. Chapter: Methodology

The main goal of this thesis is to improve the accuracy of the prediction tool in classifying preterm birth. Specifically, this thesis focuses on data preprocessing methods, to ensure the data is of the highest quality, before applying the Artificial Neural Network classifier for model evaluation. This chapter outlines the steps taken to achieve this goal.

The 8-step methodology for this work is outlined in Figure 3.1. Excluding Step 1, 4 and 5, this methodology followed closely with the work done by Ong [24]. This was done to accurately measure the effectiveness of the application of these data preparation tools, (Step 4 & 5) with the overall improvement of the classifier's ability to predict preterm birth.

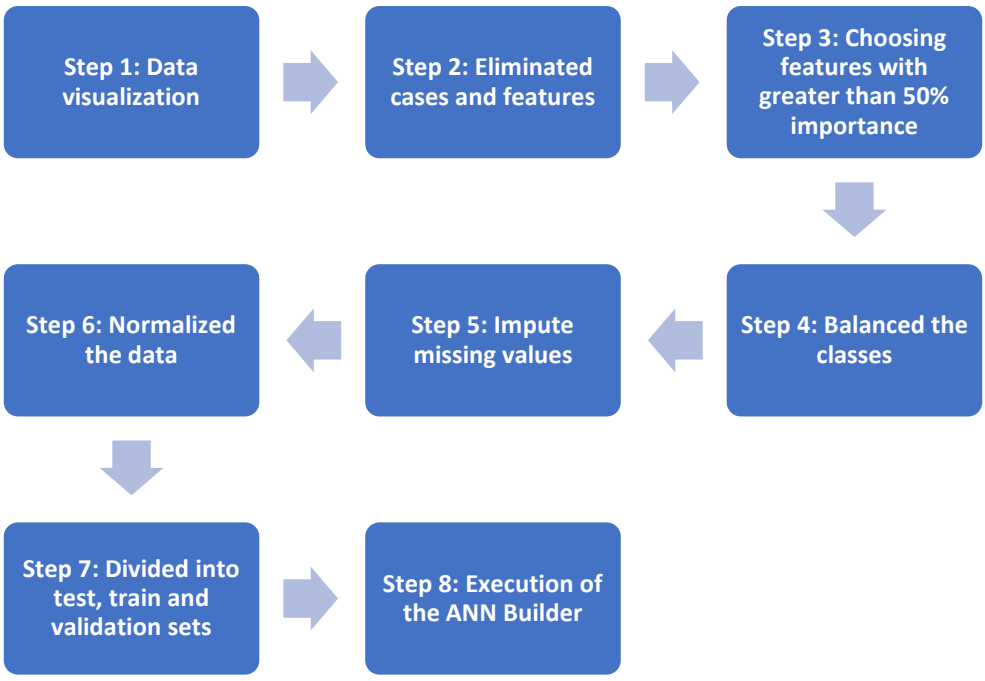


Figure 3.1. Schematic representation of the methodology used for the preterm birth classification tool

A brief description of each of the 8 steps followed is outlined in Table 3.1.

Table 3.1. Methodology for the development and evaluation of the predictive tool

Steps	Description
Step 1: Data visualization	This step was done to increase our knowledge of the features and missing values included in BORN and PRAMS, through visualization and statistical understanding.
Step 2: Eliminated cases and features	This step was done following the methodology done in past work as a data preprocessing step.
Step 3: Choosing features with greater than 50% importance using the C5.0 DT classifier	This step involved feature reduction of the numerous features included in BORN and PRAMS
Step 4: Balanced the classes	This step involved balancing the number of preterm and term cases for training of the ANN.
Step 5: Impute missing values	This step involves filling in the missing values with the reduced dataset from both BORN and PRAMS
Step 6: Normalized the data	This step involved normalizing the data in preparation for using the ANN model.
Step 7: Divided into test, train and validation sets	This step consisted of dividing the data into three sets, to prepare for model evaluation using 5-by-2 cross validation
Step 8: Execution of the ANN Builder	This step involved the training and testing of the datasets using the ANN Builder and the final evaluation of the predictive tool using the validation set.

3.1. Preliminary step: Ethics Clearance

This thesis work was approved by the Carleton University Research Ethics Committee and by the CHEO Research Ethics Board. The databases used in this thesis work were: (1) Better Outcomes Registry & Network (2010 - 2012) database (BORN) and the (2) Pregnancy Risk Assessment Monitoring System (2009-2011) (PRAMS). A contract was signed protecting the intellectual property of the data and their confidentiality before accessing both databases for this thesis.

3.2. Step 1: Data Visualization

As noted in Chapter 2, data visualizations can be useful in determining possible relationships between attributes and can provide information about individual attributes. Data visualization can also reveal noisy aspects of the data such as outliers and show clusters in the data which might indicate which is the best classifier to model the data.

The benefit of using Tableau as an analytic tool is that you can transform your data from raw values to informative graphs, such as bar charts. Bar charts were widely used for data analysis in this work because bar charts are good for showing comparisons. R was also used to visualize the missing values present in BORN and PRAMS. Before applying complex algorithms, it is important to understand the data and features present.

3.3. Step 2: Eliminating cases and features

The first step in the removal of features was to load the raw clinical data into Excel. Any missing values were denoted as ‘N/A’. Then the ‘COUNTIF’ formula was used in Excel to count the number of cells which contain missing values; from this, one could determine the percentage of missing values for each feature. All features which contained greater than 50% of missing values were removed. This followed steps taken in the theses of Ong [24] and Yu [27]. Applying

the Artificial Neural Network classifier in the final stage would require the datasets to have no missing values; the focus was to not introduce too much imputed data into the dataset, to reduce bias of the data. In addition, any cases which had a missing outcome (preterm or term) were deleted. A more detailed description of the removed features can be found in Appendix B.

It was important to only included Parous and Nulliparous features which could be known at 23 weeks gestation so that preventative treatment could be applied, and patients could be monitored to improve clinical outcomes. Both the BORN and PRAMS dataset were further divided into BORN_Parous, BORN_Nulliparous, PRAMS_Parous and PRAMS_Nulliparous datasets based on features selected by our clinical supervisor. Features which were only specific to mothers, who have had previous births, fell under the Parous category (i.e. previous premature birth). After feature and case elimination steps were applied to the raw BORN and PRAMS data, divisions between BORN_Nulliparous, BORN_Parous, PRAMS_Nulliparous and PRAMS_Parous were applied in the subsequent steps.

3.4. Step 3: Choosing features with greater than 50% importance using the C5.0 DT classifier

The C5.0 DT classifier has the capability to deal with missing values. Therefore, two options needed to be investigated:

1. Balance the data (using the ubBalance package in R), impute the missing values (using the missForest package in R), and then apply the C5.0 DT classifier for feature reduction

2. Apply the C5.0 DT classifier for feature reduction with the missing values present in BORN and PRAMS, and then carry out the preprocessing steps (balance the data and fill in missing values)

The results are summarized in the next chapter.

1. The first step in creating the C5.0 DT classifiers was to modify a file called "*mortality.names*" this file contained information about the features and classes (files are labeled as mortality/nonmortality throughout this research, due to past work done by Hasmik on the ANN Builder [13], her work was focused on neonatal mortality risk estimation models using Artificial Neural Networks)
2. In the mortality.names file the OUTCOME feature represented the target attribute, the CASE ID was the label attribute and the rest of the features in: PRAMS_Parous, PRAMS_Nulliparous, BORN_Parous or BORN_Nulliparous were defined to be continuous (numeric) or discrete (nominal).
3. The next step was to create two csv files, one labeled *mortality.csv* and the other labeled *nonmortality.csv*. The first file contained all the cases with a preterm label and the other file contained all the cases with a term label.
4. After this was done, a script called *./create_5by2_folds.sh* along with the mortality and nonmortality files were executed in the Cygwin terminal. This script automatically created 10, 5-by-2 cross validation sets.
5. The next step to create the DTs is the bash script *./run_dt_5by2.sh*. This is a command which calls C5.0 to create DTs for each of the 10 previously created sets. This produced 10 output files. The decision trees can be viewed in the mortality_fold_1_a.out and the mortality_fold_1_a.out.boost (boosting enabled) files (see Figure 3.2).

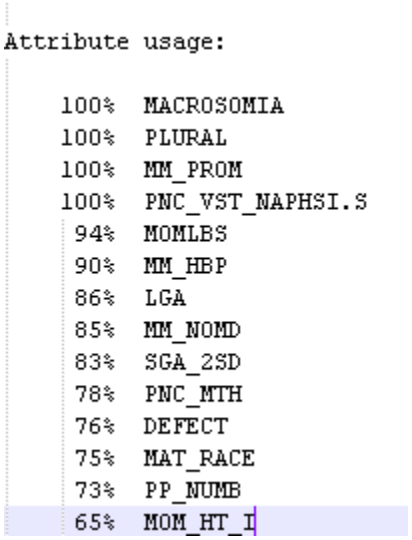


Figure 3.2. Script files representing the DT classifiers

6. Within each of the script files the percentage usage of each feature is listed (See Figure 3.3).

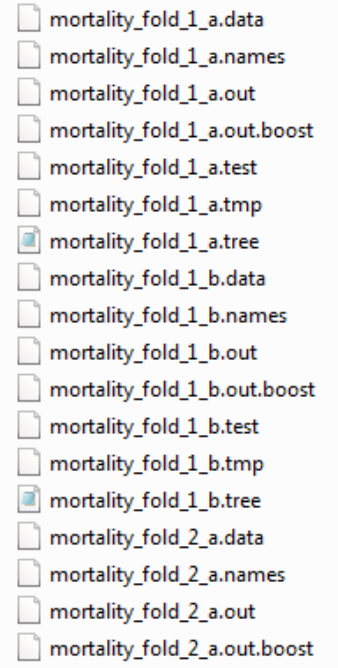


Figure 3.3. Feature percentage usage displayed

7. Across the 10, C5.0 DTs, features with high attribute percentage were repeated; the variance existed close to the threshold of 50%. The final feature subsets were chosen by averaging the percentage usage of each feature across the 10 trees and choosing features which had the highest averages and exceeded the 50% threshold. The results of the final feature subset for each of the four datasets can be found in the next chapter.

3.5.Step 4: Balancing the classes

In this research work, the unbalanced algorithm was used to apply the random undersampling technique to the clinical datasets, in R [76]. The undersampling sub-function randomly removes instances of the majority class while leaving all instances of the minority class (ubUnder package). The ubUnder type has to be selected because the ubBalance package contains both undersampling and oversampling methods. This function allows the user to determine which percentage of the majority class will be left after sampling. In this work, 50% preterm cases and 50% term cases remained in the training dataset, so the classifier could be trained with an equal proportion of both classes. The code below describes the BORN or PRAMS dataset represented as X, with the Y variable representing the final OUTCOME feature (preterm or term cases) as well as the type of balancing method (ubUnder) and the sampling parameters. The description of which parameters were selected from this function are described in Table 3.2.

```
balance_dataset ← ubBalance (X, Y, type="ubUnder", positive= 0,
perc=50, method="percPos", w=NULL, verbose=FALSE)
```

Table 3.2. Description of parameters for package in R (ubBalance)

X represents the BORN or PRAMS
Y represents the OUTCOME feature (preterm or term) in BORN or PRAMS, which must be a binary factor
type represents the balancing technique, in this research *ubUnder* was used, to remove instances of the majority class (term)
positive represents the majority class (term cases), all term labels were changed from -1 to 0, when using this function

perc represents the sampling percentage which was set to 50
method represents setting the percentage of positives to 50% after undersampling
w represents sampling the majority instances with equal weights, when w is set to *NULL*
verbose represents not printing extra information, when set to *FALSE*

3.6.Step 5: Input missing values

Before applying the ANN classifier, it was necessary to impute the missing values found within the BORN and PRAMS dataset. Random forest classifiers were used to make predictions on missing values in the BORN and PRAMS datasets. This was done by initially replacing the missing values with the mean of the non-missing values within each feature. All features were then sorted from lowest to highest, according to the amount of missing values. Then each feature was trained with a random forest algorithm and predictions were made on the missing values. This process was iterated until the difference between the previous and the new imputed matrix increased for the first time. The package used to impute the missing values was missForest [48]. The code below described inputting the BORN or PRAMS dataset with missing values (noNAs file) with the missForest algorithm applied. Then the filled in data was written to a text file once the process ended. The description of which parameters were selected from this function are described in Table 3.3.

```
tempData_noNAs <- missForest (noNAs,verbose = TRUE)

# writing the data to a text file

tempData_missF <- tempData_noNAs$ximp
```

```
write.table(tempData_missF,
"c:/MIRG/Thesis2017/missForestResults.txt", sep="\t")
```

Table 3.3. Description of parameters for package in R (missForest)

noNAs represents the BORN or PRAMS dataset with missing values
verbose represents additional output between iterations: estimated imputation error and runtime, when TRUE

3.7.Step 6: Normalizing the data

Once the above preprocessing steps were applied, the four datasets were prepared for model evaluation using the MIRG ANN classifier. Before applying this classifier, normalizing the data was done, as the ANN tends to perform better when large range differences amongst features are minimized [89]. In this work, the modified Z-score transformation equation was used to transform the values between the range of -1 and 1, based on the MIRG ANN Guide [24].

The data was normalized to fall between [-1, 1] so that the activation function in the ANN treats all features weighted equally during training. Normalization of the training, testing and validation data was automated using BASH scripts. For scaling and normalization purposes, the modified z-score transformation has been used previously in the MIRG lab [90], which scales the data between -1 and 1 is:

$$\hat{x}_i^{\,n} = \frac{x_i^{\,n} - u_i}{3\sigma_i}$$

Where x_i is the feature of interest, u_i is defined as the population mean for each feature and σ_i is defined as the population standard deviation for each feature.

This automation was done using the following steps:

a. Using SQL queries**,** the mean and standard deviation was obtained for all attributes in the BORN Parous, BORN Nulliparous, PRAMS Parous and PRAMS Nulliparous features. The mean and standard deviation values were written to a file named “normalization.csv”.
b. Each dataset (BORN_Parous, BORN_Nulliparous, PRAMS_Parous and PRAMS_Nulliparous) was divided into files called “mortality” and “nonmortality” csv files
c. The mortality.csv file contained the balanced preterm cases with missing values imputed and the nonmortality.csv files contained the balanced term cases with missing values imputed.
d. Most of the values within each feature fell between the ranges of 1 to 5 as many of the features within these datasets were categorical, however, some of the continuous features such as maternal age had values of greater than 40. When looking at the dataset as a whole these values might be considered as outliers, however, the information within these features is valuable for predicting preterm birth. Therefore, normalization was done column-wise for each feature to ensure that the values fit the range of -1 to 1 and all values were included and not dropped.
e. A temporary file was created for both the mortality and the nonmortality cases. The modified z-score was calculated for each attribute column in mortality and nonmortality. This was done by obtaining the mean in the first row of the attribute column and then the second row contained the standard deviation for that attribute column. Once these two statistics were

obtained, using equation (1) above, the column data was normalized. In these temporary files, both the Case ID and Outcome features were excluded because these values should not be normalized.

f. Once all the feature columns were normalized, the data were combined into a single csv file with the untouched Case ID and Outcome features.

3.8.Step 7: Divide into train, test and verification sets

There are three divisions of the data which are defined. First, the training set is the data that trains the classifier, to improve the overall accuracy of classifying preterm and term cases. The test set is the data which is not a part of the training set and is tested by the classifier during model evaluation. Lastly, the verification set is the data which is unseen before inputting the data into the neural network model (data preprocessing is still applied to these cases). The purpose of this verification set is to output the true performance of the classifier, with data that it has not been trained or tested on, to minimize overfitting. These three sets were created using 5-by-2 Cross Validation which is described below in Table 3.4. **Separate from these three divisions**, a final test of the neural networks was evaluated on validation sets which consisted of unlabeled data and contained 7.9% prevalence to match the population.

Table 3.4. Division of train, test and verification sets

Training Set	Testing Set	Verification Set
50% of the dataset	25% of the dataset	25% of the dataset

3.8.1. 5-by-2 Cross Validation

This work used 5-by-2 Cross Validation, to reduce overfitting of the classifier during the training stage. Also, creating 10 sets of training, test and verification data with an equal number of

preterm and term cases; to ensure sufficient data was being verified by the ANN model. Before using the ANN classifier, the clinical datasets were first normalized using the modified z-score formula. BASH files have been developed by Gilchrist [91] to carry out 5-by-2 cross validation. A BASH script file called create_5_by_2.sh carried out the following steps:

PHASE 1: There are two files one which contains the preterm cases and another file which contains the term cases.

PHASE 2: Preterm and term cases are randomized and divided between Set A and Set B. At this point the preterm and term cases remain separate.

PHASE 3: Set A which contains both preterm and term cases is further divided between two cases (A1 and A2) while Set B remained unchanged. At this point A1, A2 and B contain preterm and term cases. The subset of data is now 50% training, 25% test and 25% verification.

PHASE 4: The above process is reversed where Set B (containing preterm and term cases) is further divided between two cases (B1 and B2) while Set A remains unchanged and the same ratio is present.

PHASE 5: As a result of PHASE 3, Set #1 is produced which consists of B, A1, and A2 for the training, test and the verification set respectively. While PHASE 4 results in Set #2 which consists of A, B1 and B2. This process is repeated five times to create a total of 10 sets of training, test and verification data

These steps ensure preterm and term cases are divided into equal parts and therefore there exists an equal number of preterm and term cases for train, test and verification of the DT and ANN models. These steps are summarized in Figure 3.4.

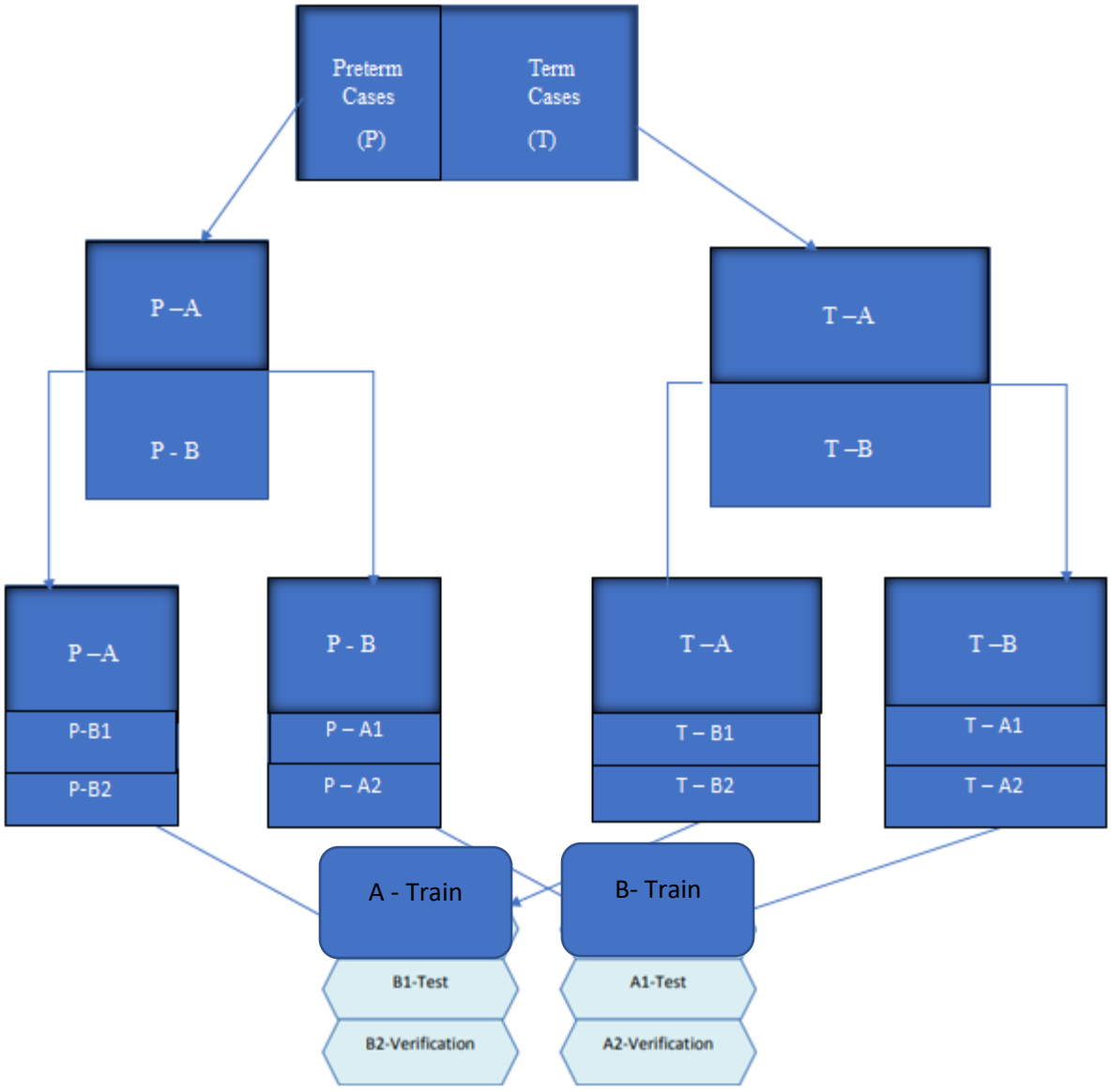


Figure 3.4. 5-by-2 Cross Validation to create train, test and verification sets

3.9. Step 8: Execution of the ANN Builder

The purpose of this research was to follow similar steps applied, in the methodology of previous work, to compare the difference in sensitivity results for preterm birth predictions when focusing on data preparation. Therefore, the same ANN Builder using the FANN library, was used from past research [7].

1. These steps were repeated for all four datasets.
2. The ANN Builder software was used to run the ANN Classifier and carried out training and testing of the data.
3. The following network structures were automatically detected by the software for training (see Figure 3.5): the number of hidden layers, the number of inputs (this is dependent on the number of features determined by the C5.0 Decision Tree Classifier) and the number of outputs is 1 (term or preterm).

```
MIRG ANN Builder v1.3.0 - April 7, 2015
Run_20803
Start Time: Fri Aug 10 15:57:10 2018

Data information
--------------------
Number of cases is 82186
Number of features is 17
--------------------

Network structure
--------------------
Number of layers is 3
Number of inputs is 17
Number of outputs is 1
--------------------

User inputs
--------------------
Running mode is (1=fast, 2=medium, 3=slow) 1
Subparameter mode is (0=off) 0
Network selection thresholds are:
Test_Sn Test_Sp Ver_Sn Ver_Sp: 85 75 85 75
Stopping the loop: 0
Thresholds for stopping: 0 0
--------------------

Dividing cross validation sets or hidden nodes
--------------------
Cross validation range is [1,10]
```

Figure 3.5. Parameters for the BORN_Nulliparous dataset

4. After balancing the classes there were 102,187 cases in the BORN dataset and 46,867 cases in the PRAMS dataset. From this, 20,001 cases from BORN, and 10,001 cases from PRAMS were put aside for the final testing stage of the validation set. Therefore, the BORN dataset had around 82,186 cases to be trained and the PRAMS dataset had around 36,866 cases to be trained with the ANN model.
5. The threshold to save the networks was chosen to be 60-85% for sensitivity and 70-75% for specificity; these were the tested highest thresholds which would save the networks in the result files.

6. The choice to optimize sensitivity over specificity was selected when selecting the best networks and the performance metrics from the results were saved in a separate CSV file (classifier_stats_final.csv).
7. The ANN Builder will create 10 networks which optimize the sensitivity metric
8. This final validation set is separate from the training, testing and verification sets created from 5-by-2 cross validation. The validation set consisted of 5,000 cases (4605 term and 395 preterm) for PRAMS_Parous and PRAMS_Nulliparous and 10,000 (9210 term and 790 preterm) cases for BORN_Parous and BORN_Nulliparous. This validation set had the labels removed before inputting the data into the ANN model for final classification of the output labels. These cases were aggregated by randomly sorting rows in Excel and selecting 790 or 395 preterm cases.
9. The performance metrics were calculated (sensitivity and specificity) for these four datasets and are described in detail in the next section

Execution of the ANN Builder software was used with the following parameters: FAST mode (tests around 0.5% of all possible combinations, excluding the number of hidden nodes), 3 hidden layers and the reported above network thresholds (see Step 5).

Another script was created: The Performance Measures Calculation Tool [13] for outputting the performance metrics of the best network. These metrics include the Positive Predictive Value (PPV), Negative Predictive Value (NPV), Accuracy (ACC), Matthews Correlation Coefficient (MCC), Receiver Operating Curve (ROC), F1-Score and Area Under the Curve (AUC). These statistical metrics were saved in the classifier_stats_final.csv.

The ANN Model Selection Tool [13] is a script which was used to select the best performing network based on the highest sensitivity. This selection script is applied to 10 result files (after 5-

by-2 cross validation) and sorts through to find the final network with the highest sensitivity, within the verification and test sets. This final network was tested against the validation set (which is separate from the three datasets created from 5-by-2 Cross Validation and consists of 10,000 BORN or 5,000 PRAMS cases). More details regarding the network parameters can be found in Appendix C.

4. Chapter: Results and Discussion

This chapter outlines the results of this thesis using data preparation methods and machine learning classifiers. The results stem from the C5.0 DT Classifier for feature reduction and the Artificial Neural Network Classifier for model evaluation.

Table 4.1. Results for the development and evaluation of the predictive tool

Steps	Results
Step 1: Data Visualization	Bar charts and plots showing the missing values within the data
Step 2: Eliminated cases and features	Removed cases with greater than 50% missing values and no outcome label
Step 3: Choosing features with greater than 50% importance using the C5.0 DT classifier	Justified the 50% threshold and reduced feature subsets were output across the 4 datasets.
Step 4: Balanced the classes	Created an equal number of preterm and term cases for training of the ANN using ubBalance.
Step 5: Impute missing values	Filled in missing values using missForest
Step 6: Normalized the data	Normalized the data in preparation for using the ANN model.
Step 7: Divided into test, train and verification sets	Training, testing and verification sets for the ANN model.
Step 8: Execution of the ANN Builder	Created optimal networks for the final testing stage and performance metric results outputted

4.1.Step 1: Data Visualization

The bar chart in Figure 4.1 compares a variety of clinical features: OTH_Term (Pregnancy history: other terminations?), Plural (Plurality births), Preghx (Pregnancy history: calculated from calculated from Previous Live Birth, Previous Low Birth Weight birth, and Previous Preterm birth), Prev_Lb (Previous live births) plotted against the Outcome feature (1 for a preterm outcome and -1 for a term outcome).

The small average difference between the Parous features reveals that there might not be a significant difference between these Parous clinical features and a preterm or term outcome. Therefore, more advanced algorithms are needed such as the C5.0 DT classifier to determine features of importance. However, the benefit of using Tableau is that it provides a visual basis to have conversations about features with our clinical partner, instead of looking at raw data from Excel.

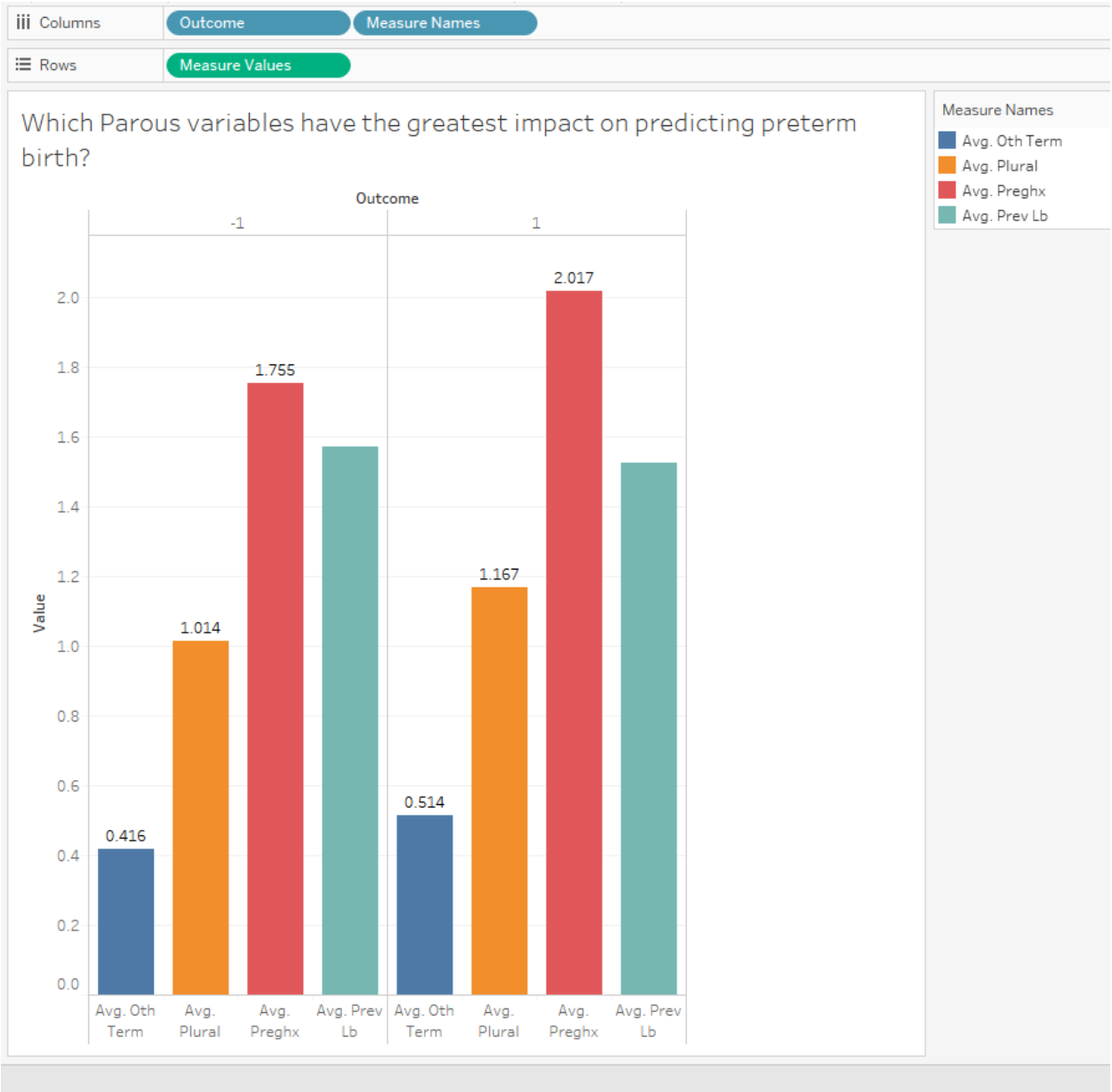


Figure 4.1. Bar Chart in Tableau comparing Parous_PRAMS features

Missing values were quite prevalent within both the BORN and PRAMS dataset. The below Missingness Maps (Figure 4.2 & 4.3) were created to quickly see the presence of missing values within the clinical features using the Amelia package in R [92]. The x-axis lists the features from the BORN or PRAMS dataset and the y-axis is the CASE ID. Comparing the same number of cases (50) the BORN dataset seems to have more missing values present than the PRAMS

dataset, although this could be dependent on the specific features compared. Using more complex algorithms such as missForest are necessary when analyzing the missing values in detail. However, the benefit of using these maps is that it gives the user a quick insight into the general number of missing values present.

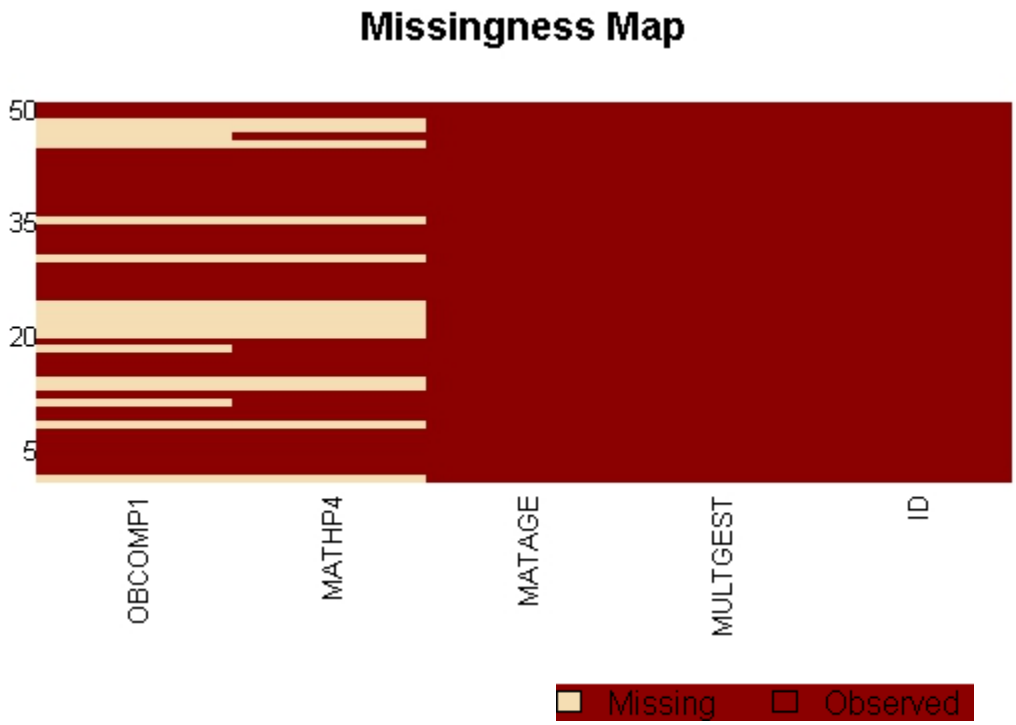


Figure 4.2. Missingness Map for the BORN_Nulliparous features

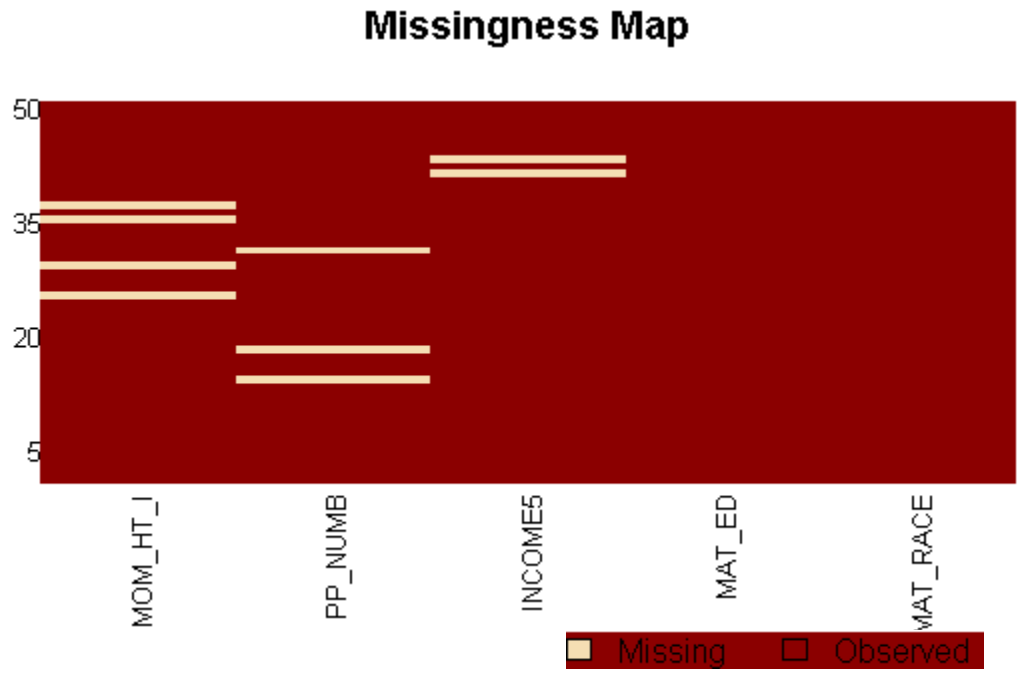


Figure 4.3 Missingness Map for the PRAMS_Nulliparous features

4.2.Step 2: Eliminating Cases and Features

Preliminary data preparation was done in Excel to remove features with greater than 50% missing values and missing OUTCOME labels, the final results are displayed in Table 4.2.

Table 4.2. Number of features prior to and after feature and case elimination

	Before Feature and Case Elimination	After Feature and Case Elimination
PRAMS	# Features: 372 # Cases: 109,319	# Features: 81 # Cases: 109,076
BORN	# Features: 226 # Cases: 679,697	# Features: 200 # Cases: 669,134

4.3.Step 3: Choosing features with greater than 50% importance using the C5.0 DT classifier

As previously stated, the C5.0 DT classifier has the capability to deal with missing values. This led to investigating whether one should fill in missing values before or after feature reduction. Although the sensitivity results were initially higher during training with the imputed values, (see Table 4.3), the final results show that when testing the classifier, the classifier performed generally worse. Therefore, it was decided to determine the features of importance prior to imputing the missing values, to reduce possible overfitting of the results.

Table 4.3. Comparison of the two methodologies

PRAMS Nulliparous Dataset	**Option 1**	**Option 2**
Training Set (Sensitivity)	79±0%	76±0%
Test Set (Sensitivity)	74±1%	74±1%
PRAMS Parous Dataset	**Option 1**	**Option 2**
Training Set (Sensitivity)	79±1%	77±0%
Test Set (Sensitivity)	72±1%	74±0%
BORN Parous Dataset	**Option 1**	**Option 2**
Training Set (Sensitivity)	88±0%	87±0%
Test Set (Sensitivity)	82±0%	87±0%
BORN Nulliparous Dataset	**Option 1**	**Option 2**
Training Set (Sensitivity)	88±0%	87±2%
Test Set (Sensitivity)	82±0%	87±0%

The 50% threshold was determined experimentally by testing different feature subset sizes using the C5.0 DT classifier. It was found that including features with greater than 30% feature importance, sometimes resulted in slightly lower classification performance and greater computational time (see Table 4.4. & 4.6.). Another test included features with greater than 65% importance (see Table 4.5 & 4.7.). This resulted in a slight increase in accuracy, but this threshold resulted in the removal of clinical features deemed important by our clinician supervisor for predicting preterm birth, such as the feature, SGA_10 (small for gestation age) in the PRAMS dataset and INTBF (intention to breastfeed) in the BORN dataset. Therefore, to maintain a good balance, between including key clinical features and high accuracy, a feature importance threshold of ≥ 50% was selected.

Table 4.4. Increased feature size to include ≥ 30% feature importance (BORN)

Performance Metric	Train	Test	Standard Deviation
Accuracy:	0.85	0.84	±0.00
Sensitivity/Recall:	0.91	0.90	±0.01
Specificity:	0.78	0.78	±0.01

Table 4.5. Reduced feature size to include ≥ 65% feature importance (BORN)

Performance Metric	Train	Test	Standard Deviation
Accuracy:	0.84	0.84	±0.00
Sensitivity/Recall:	0.91	0.90	±0.01
Specificity:	0.77	0.77	±0.01

Table 4.6. Increased feature size to include ≥ 30% feature importance (PRAMS)

Performance Metric	Train	Test	Standard Deviation
Accuracy:	0.84	0.84	±0.01
Sensitivity/Recall:	0.91	0.91	±0.01
Specificity:	0.77	0.76	±0.03

Table 4.7. Reduced feature size to include ≥ 65% feature importance (PRAMS)

Performance Metric	Train	Test	Standard Deviation
Accuracy:	0.85	0.85	±0.00
Sensitivity/Recall:	0.92	0.92	±0.01
Specificity:	0.77	0.76	±0.01

The C5.0 DT classifier outputs the percentage attributes of the features of importance without any preprocessing methods being applied to the data. It was important to not manipulate the data

so that, when the ANN classifier encounters new test data, this does not result in the classifier overfitting the data.

The C5.0 DT classifier outputs ten trees and displays the feature importance for each tree. To maintain a good balance between the importance and the quantity of features chosen for each dataset, only features which had ≥50% feature importance were kept. Although most features had the same percentage attribute across all ten of the trees such as the features: PLURAL and MULTGEST (100%), there were some features that differed among the ten trees which were close to the 50% threshold. In these cases, features were averaged across the ten trees and the feature with the highest percentage average was chosen.

There were some obvious features that were selected by the classifier such as GENDER (baby's sex) and PPRETERM (number of previous preterm babies) in the BORN dataset and MAT_AGE_NAPHSIS (maternal age grouped) and MAT_RACE (maternal race) in the PRAMS dataset. These features have been documented to be increased risk factors for a preterm birth outcome [30]. Some non-obvious features that were selected included PRENCLAS (number of prenatal classes in weeks) and INTBF (intention to breastfeed) in the BORN dataset and MAT_ED (maternal education) and PP_NUMB (# sources of payment for prenatal classes) in the PRAMS dataset, these non-obvious features might allude to a certain socioeconomic status, leading to an increased/decreased risk of preterm birth.

Once these features were reduced from over 300 features in PRAMS and over 200 features in BORN (Table 4.8), this significantly decreased processing time and more importantly increased the sensitivity results; as the subset of features chosen, were directly important to predicting a preterm birth outcome.

Table 4.8. Feature reduction results after applying the C5.0 DT classifier to the BORN and PRAMS datasets

Datasets	Before Feature Reduction	After Feature Reduction
BORN_Parous	# Features: 200	# Features: 20
BORN_Nulliparous	# Features: 180	# Features: 17
PRAMS_Parous	# Features: 81	# Features: 22
PRAMS_Nulliparous	# Features: 75	# Features: 20

The following Tables 4.9- 4.12 display the reduced features subsets (threshold of $\geq 50\%$) output by the C5.0 DT classifier for BORN and PRAMS

Table 4.9: 20 Features: Parous BORN

100% MULTGEST: multiple gestation	95% PRENCLAS: Prenatal class
95% CONGAN55: Anomalies unclassified elsewhere - Other syndromes	80% GENDER: Baby's sex
82% OBCOMP12: Preterm premature rupture of membranes (PPROM)	74% OBCOMP1: Obstetrical complications (Eclampsia)
76% PREVCS: Previous cesarean Section	74% OBCOMP9: Pre-eclampsia
74% OBCOMP8: Obstetrical complications (Placental abruption)	70% OBCOMP7: Obstetrical complications (Placenta previa)
71% OBCOMP4: IUGR/SGA (Small for gestational age)	69% OBCOMP10: Premature rupture of membranes (PROM)
69% PPRETERM: Number of previous preterm babies	64% OBCOMP3: Hypertension (gestational or transient)
64% MATAGE: Mother's age (years)	61% MATHP27: Other Maternal Health Problem

62% MATHP4: Maternal health problem (Diabetes insulin)	60% MATHP3: Chronic hypertension
55% OBCOMP5: Obstetrical complications (Large for Gestational Age)	50% INTBF: Intention to Breastfeed

Table 4.10: 17 Features: Nulliparous BORN

100% MULTGEST	80% GENDER
80% PRENCLAS	79% OBCOMP12
77% CONGAN55	76% MATAGE
74% OBCOMP1	74% OBCOMP8
74% OBCOMP9	70% OBCOMP4
69% OBCOMP7	68% OBCOMP10
65% MATHP27	62% OBCOMP3
62% MATHP3	57% MATHP4
58% OBCOMP5: LGA (large for gestational age)	

Table 4.11: 22 Features: Parous PRAMS

100% PLURAL: plurality	100% MM_PROM: rupture membrane?
99% PNC_VST_NAPHSIS: number of prenatal care visits grouped	93% MM_HBP: hypertension?
87% PREGHX: pregnancy history	84% MOMLBS: maternal weight gain
84% SGA_2SD: small for gestational age based on 2SD from mean	83% LGA: large for gestational age based on 90th percentile

83% PNC_MTH: month of first prenatal care visit	79% DEFECT: defect present? (this can be detected during an antenatal ultrasound)
82% MM_FEVER: fever (mother)?	76% MAT_RACE: maternal race
77% OTH_TERM: pregnancy history (other terminations?)	72% MOM_HT_I: mom total height (inches)
73% BC_YRLLB: years since last live birth	67% PNC_WKS: weeks 1st prenatal care visit
71% INCOME5: 12 months before, total income	64% MM_NOMD: no medical risk factors?
66% PRE_LB_NAPHSIS: number of previous live births grouped	61% SGA_10: small for gestational age based on 10th percentile
54% PP_NUMB: # sources of payment for prenatal care	51% MAT_ED: maternal education

Table 4.12: 19 Features: Nulliparous PRAMS

100% PLURAL	100% MM_PROM
100% MACROSOMIA: Macrosomia: $\geq$ 4500 gram birth weight	100% PNC_VST_NAPHSIS
90% MM_HBP	88% LGA
87% MOMLBS	85% SGA_2SD
81% INCOME5	81% MM_NOMD:
79% PNC_MTH	79% DEFECT

78% MM_FEVER	78% MAT_RACE
77% MAT_ED: maternal education	78% MOM_HT_I
67% PP_NUMB: # sources of payment for prenatal care	56% MAT_AGE_NAPHSIS: maternal age grouped
51% SURE_WKS: weeks when sure pregnant	

There are several similar features chosen by the C5.0 DT classifier between the PRAMS and BORN datasets (see Figure 4.4.) Despite the differences, which include how the data has been obtained, the features which have been measured, and the location of the clinical datasets, this classifier has determined key features of importance when predicting a premature birth. These features are important to record if one wants to build their own preterm birth dataset specific to a clinical site. By inputting these features into the neural network, there is a high probability of improved sensitivity results. Some of these features include: maternal age, if the mother has high blood pressure, presence of previous premature births etc.… There are also similar features chosen between Ong's research work [24] (see Table 4.13-4.16). These features are of importance when predicting preterm birth, as they tend to appear across various research reports on preterm birth.

BORN	PRAMS
MULTGEST: multiple gestation	PLURAL: plurality
OBCOMP10 & OBCOMP12: premature rupture of membranes (PROM) & Preterm premature rupture of membranes (PPOM)	MM_PROM: ruptured membranes?
OBCOMP4: Small for gestational age	SGA_2SD & SGA_10: Small for gestational age based on 2 standard deviation from the mean & Small for gestational age based on 10^{th} percentile
OBCOMP5: Large for gestational age	LGA: Large for gestational age based on the 90^{th} percentile
MATAGE: Mother's age in years	MAT_AGE_NAPHSIS: Maternal age grouped
PPRETERM: Number of previous preterm babies	PREGHX: Pregnancy history (calculated from Previous Live Birth, Previous Low Birth Weight birth, and Previous Preterm birth)
OBCOMP3 & MATHP3 (Hypertension gestational or transien & Chronic hypertension	MM_HBP: Hypertension?

Figure 4.4. List of abbreviations used for highly ranked features which occurred in both the BORN and PRAMS data sets, used in this study to assess risk of preterm birth

Table 4.13: Similar features chosen in current and earlier research work: Parous_BORN

100% MULTGEST	95% PRENCLAS
95% CONGAN55	80% GENDER
82% OBCOMP12	74% OBCOMP1
76% PREVCS	74% OBCOMP9
74% OBCOMP8	70% OBCOMP7
71% OBCOMP4	69% OBCOMP10
69% PPRETERM	64% OBCOMP3
64% MATAGE	61% MATHP27
62% MATHP4	60% MATHP3
55% OBCOMP5	50% INTBF

These features were also present in past work

Table 4.14: Similar features chosen in current and earlier research work: Nulliparous_BORN

100% MULTGEST	80% GENDER
80% PRENCLAS	79% OBCOMP12
77% CONGAN55	76% MATAGE
74% OBCOMP1	74% OBCOMP8
74% OBCOMP9	70% OBCOMP4
69% OBCOMP7	68% OBCOMP10
65% MATHP27	62% OBCOMP3
62% MATHP3	57% MATHP4
58% OBCOMP5	

These features were also present in past work

Table 4.15: Similar features chosen in current and earlier research work: Parous_PRAMS

100% PLURAL: plurality	100% MM_PROM: rupture membrane?
99% PNC_VST_NAPHSIS: number of prenatal care visits grouped	93% MM_HBP: hypertension?
87% PREGHX: pregnancy history	84% MOMLBS: maternal weight gain
84% SGA_2SD: small for gestational age based on 2SD from mean	83% LGA: large for gestational age based on 90th percentile
83% PNC_MTH: month of first prenatal care visit	79% DEFECT: defect present? (this can be detected during an antenatal ultrasound)
82% MM_FEVER: fever (mother)?	76% MAT_RACE: maternal race
77% OTH_TERM: pregnancy history (other terminations?)	72% MOM_HT_I: mom total height (inches)
73% BC_YRLLB: years since last live birth	67% PNC_WKS: weeks 1st prenatal care visit
71% INCOME5: 12 months before, total income	64% MM_NOMD: no medical risk factors?
66% PRE_LB_NAPHSIS: number of previous live births grouped	61% SGA_10: small for gestational age based on 10th percentile
54% PP_NUMB: # sources of payment for prenatal care	51% MAT_ED: maternal education

These features were also present in past work

Table 4.16: Similar features chosen in current and earlier research work: Nulliparous_PRAMS

100% PLURAL	100% MM_PROM
100% MACROSOMIA: Macrosomia: ≥ 4500 gram birth weight	100% PNC_VST_NAPHSIS
90% MM_HBP	88% LGA
87% MOMLBS	85% SGA_2SD
81% INCOME5	81% MM_NOMD:
79% PNC_MTH	79% DEFECT
78% MM_FEVER	78% MAT_RACE
77% MAT_ED: maternal education	78% MOM_HT_I
67% PP_NUMB: # sources of payment for prenatal care	56% MAT_AGE_NAPHSIS: maternal age grouped
51% SURE_WKS: weeks when sure pregnant	

These features were also present in past work

4.4.Step 4: Balancing the Classes

When applying this function, this greatly reduced the number of cases in the training dataset (See Table 4.17.) and improved the computational training time of the neural network. For instance, in work done by Ong [24], the BORN_Parous and BORN_Nulliparous datasets took around 634 hours and 186 hours respectively to train, whereas the PRAMS_Parous and PRAMS_Nulliparous took 73 and 36 hours respectively to train. In this work, with the reduction of the dataset, the BORN_Parous and BORN_Nulliparous datasets took around 10 and 9 hours respectively to train, whereas the PRAMS_Parous and PRAMS_Nulliparous took around 4 hours each to train. The hardware specifications of the computers on which the models were trained on were similar.

All simulations in this current work were run on BME-12 lab computers: Intel Core i5 760 (2.80GHz) processor, 8GB RAM, Windows 7 64bit. Where Ong [24], ran her models on the BME-12 and BME-14 lab computer: Intel Core i7-3770 (3.4GHz) processor, 8 GB RAM, Windows 7 64bit.

Table 4.17. Case reduction results after applying package in R (ubBalance) to the BORN and PRAMS datasets

	Before Class Balance	After Class Balance
BORN	# Cases: 679,697	# Cases: 102,187
PRAMS	# Cases: 109,079	# Cases: 46,867

4.5.Step 5: Input missing values

As stated previously, missForest uses random forest classifiers. These classifiers do not need to perform 5-by-2 cross validation to create a test set such as with the DT classifier or with the ANN classifier because random forests contain internal test sets to estimate the error. During the random forest run around 1/3 of cases are not used during training and are instead used as a test set. The out of bag (OOB) imputation error supplied two values for the categorical and nominal features and the results are displayed in Table 4.18. The proportion of falsely classified (PFC) cases represents the error for the categorical features and the normalized mean square error (NMSE) represents the error for the nominal features [48].

Table 4.18 OOB error estimate for Nulliparous_PRAMS dataset

NRMSE: 0.2353279	PFC: 0.3191449

4.6.Step 6: Normalizing the data

Results from normalizing the data using the modified Z-score transformation are displayed in Figure 4.5., saved in a .data file. The data is scaled between a range of -1 to 1.

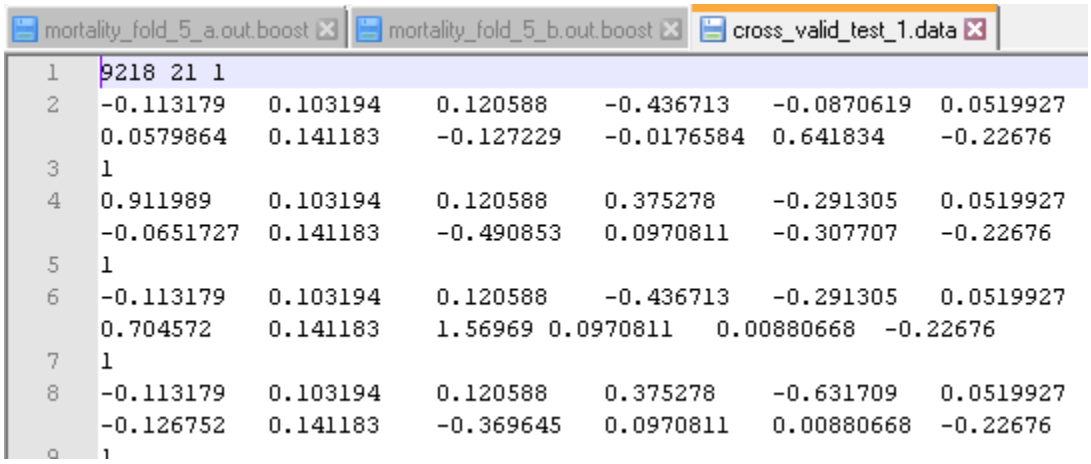


Figure 4.5. Results of data normalization

4.7.Step 7: Divide into test, train and verification sets

The results from applying the BASH file ./create_5_by_2.sh are displayed in the below Figure 4.6. Once these files have been created, then the training of the neural networks using the ANN builder [13] can commence.

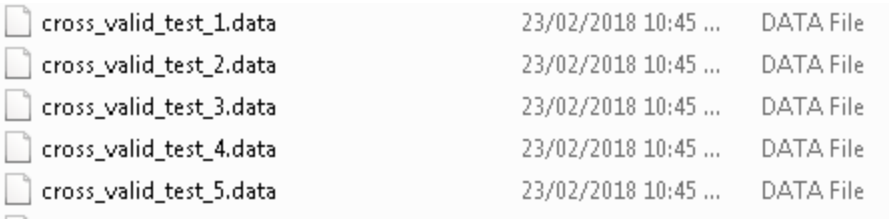


Figure 4.6. Results of 5-by-2 Cross Validation (test set)

4.8. Step 8: Execution of the ANN Builder

After 5-by-2 cross validation was applied to create train, test and verification sets for the ANN, around 100 neural networks were saved in the network folders and the best neural network which optimized sensitivity was selected. An example of the performance metrics for the PRAMS_Parous classifier is displayed below in Table 4.19. This neural network was then tested

on the validation set for final testing. The validation set for the BORN dataset consisted of 10,000 cases set aside for final testing. Similarly, the validation set for the PRAMS dataset consisted of 5,000 cases set aside for final testing, A division of the data is described in Figure 4.7. The OUTCOME feature for the validation sets was removed and unlabeled data was fed into the ANN, to determine the predictive performance of the classifier. Both of these validation sets had 7.9% prevalence to match the population of preterm birth in Ontario.

Table 4.19. Performance Metrics for the PRAMS_Parous classifier

	Average	Standard deviation
Sensitivity	0.703364	0.006915
Specificity	0.734787	0.009838
PPV	0.726267	0.005978
NPV	0.712427	0.003266
ACC	0.719076	0.003314
MCC	0.438422	0.006682
F1score	0.714586	0.003064
AUC	0.788326	0.0041

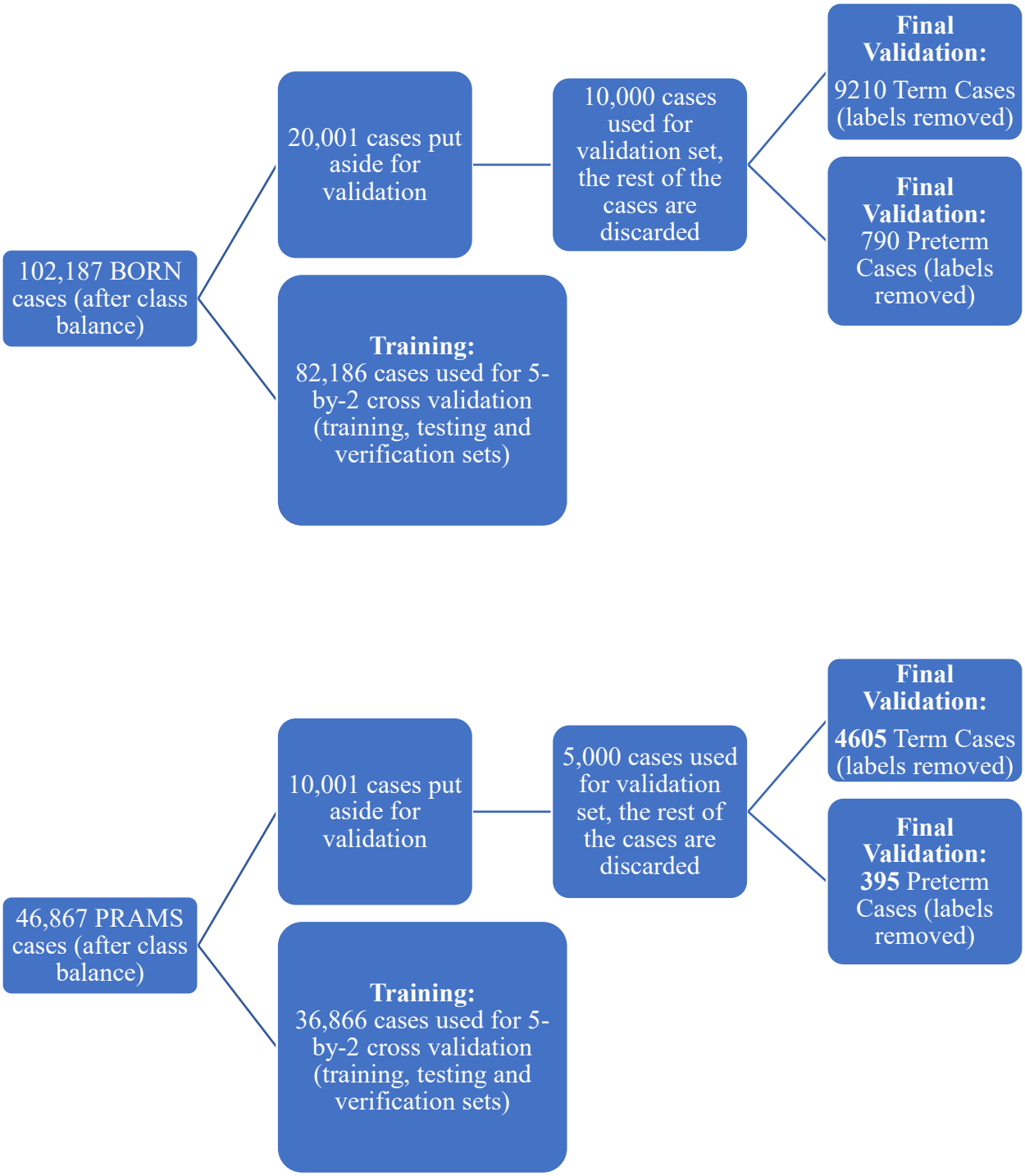


Figure 4.7 Division of the BORN and PRAMS dataset: training, testing, verification and validation data

The confusion matrix was calculated for each of the four datasets which were tested against the final validation set (10,000 for BORN and 5,000 for PRAMS) the confusion matrix, sensitivity and specificity metrics are displayed below (Table 4.20-4.27). In an imbalanced dataset which is what the ANN is tested on with 7.9% prevalence, the accuracy metric is not the most effective measure for determining the performance of the classifier. Since there is such a small proportion of preterm cases, the classifier might not be able to distinguish between the preterm cases (low true positive rate) but could instead classify the term cases with a high accuracy (high true negative rate) leading to an overall high accuracy metric. A better metric to compare the classifier's performance is the AUC (area under the curve) which aggregates the classifier performance at a variety of thresholds. In addition, due to this class imbalance there are many term cases which could be classified as false positives (falsely classified as preterm), this contributes to the low precision value (1) reported in the below tables. Conversely, due to the high number of term cases, there are few preterm cases which could be classified as term, the focus of this research is to limit this occurrence and contributes to the high negative predictive value (2) reported in the below tables.

$$PPV = \frac{TP}{TP+FP} \times 100 \text{ (1)}$$

$$NPV = \frac{TN}{TN+FN} \times 100 \text{ (2)}$$

Table 4.20. Confusion Matrix: Parous_BORN Verfication Results at 7.9% Prevalence Unlabeled Data

	Predicted Term	**Predicted Preterm**
Actual Term	TN:6241	FP: 2969
Actual Preterm	FN:85	TP: 705

Sensitivity = 89.2%

Specificity = 67.8%

Table 4.21. Performance Metrics: Parous_BORN Verfication Results at 7.9% Prevalence Unlabeled Data

Accuracy	0.69
Sensitivity/Recall	0.89
Specificity	0.68
PPV/Precision	0.19
NPV	0.99
MCC	0.32

Table 4.22. Confusion Matrix: Nulliparous_BORN Verfication Results at 7.9% Prevalence Unlabeled Data

	Predicted Term	**Predicted Preterm**
Actual Term	TN:6584	FP: 2626
Actual Preterm	FN:87	TP: 703

Sensitivity = 89.0%

Specificity = 71.5%

Table 4.23. Performance Metrics Nulliparous_BORN Verfication Results at 7.9% Prevalence Unlabeled Data

Accuracy:	0.73
Sensitivity/Recall:	0.89
Specificity:	0.72
PPV/Precision:	0.21
NPV:	0.99
F1 score:	0.34
MCC:	0.35

Table 4.24. Confusion Matrix: Parous_PRAMS Verfication Results at 7.9% Prevalence Unlabeled Data

	Predicted Term	**Predicted Preterm**
Actual Term	TN:3288	FP: 1317
Actual Preterm	FN:63	TP: 332

Sensitivity = 84.1%

Specificity = 71.4%

Table 4.25. Performance Metrics: Parous_PRAMS Verfication Results at 7.9% Prevalence Unseen Data

Accuracy:	0.73
Sensitivity/Recall:	0.84
Specificity:	0.71
PPV/Precision:	0.21
NPV:	0.99
F1 score:	0.34
MCC:	0.35

Table 4.26. Confusion Matrix: Nulliparous_PRAMS Verfication Results at 7.9% Prevalence Unseen Data

	Predicted Term	**Predicted Preterm**
Actual Term	TN:3501	FP: 1104
Actual Preterm	FN:64	TP: 331

Sensitivity = 83.8%

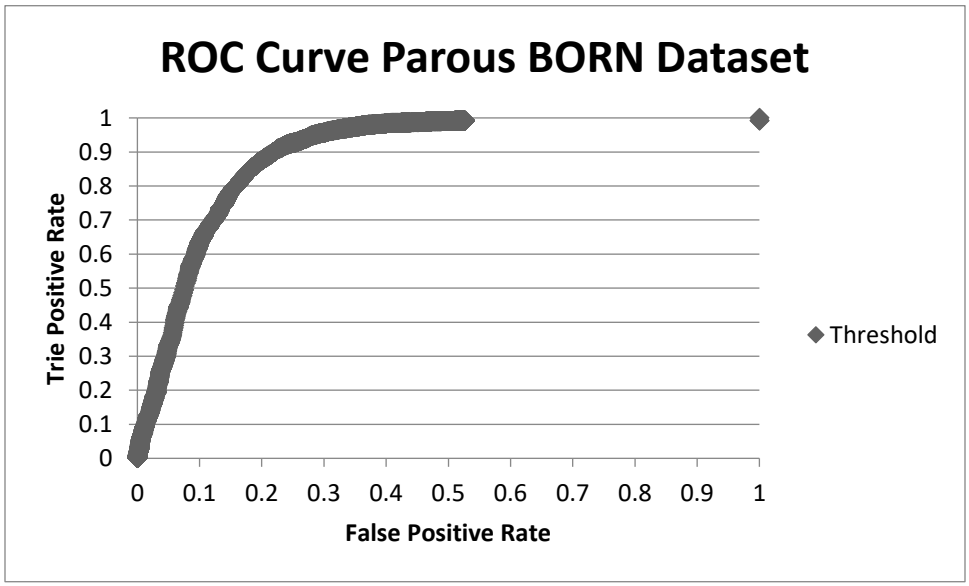
Specificity = 76.0%

Table 4.27. Performance Metrics: Nulliparous_PRAMS Verfication Results at 7.9% Prevalence Unseen Data

Accuracy:	0.77
Sensitivity/Recall:	0.84
Specificity:	0.76
PPV/Precision:	0.23
NPV:	0.98
F1 score:	0.37
MCC:	0.36

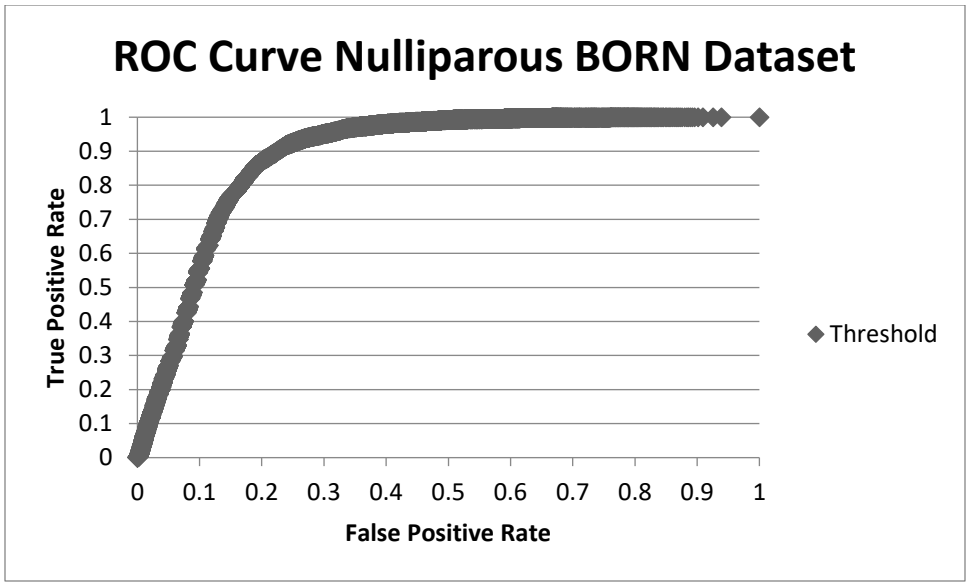
The ROC Curves for each dataset (Figure 4.8 – 4.11) are displayed below. The True Positive Rate (Sensitivity) is displayed on the y-axis and the False Positive Rate (1-Specificity) is displayed on the x-axis. Each point on the ROC curves represents the Sensitivity versus 1-

Specificity at a specific threshold (e.g. 0,0.01…1). The AUC is a measure of how accurate the classifier predictions are in predicting preterm birth, all of the curves (Figure 4.2-4.5) tend to fall under the category of "Acceptable" (> 0.7) or "Excellent" (> 0.8) when measuring the effectiveness of these classifiers.



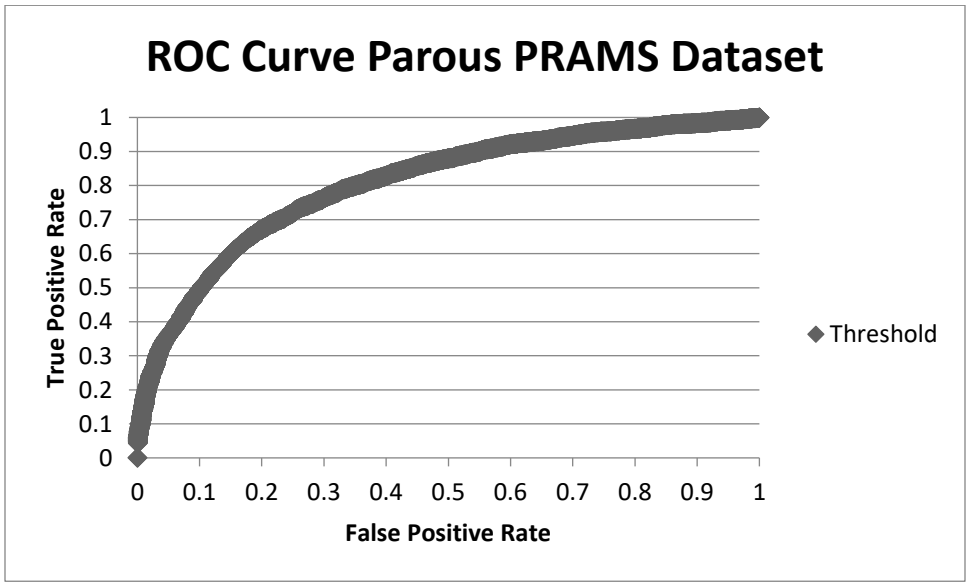
AUC: 0.894369

Figure 4.8. ROC Curve Performance for BORN Parous Dataset



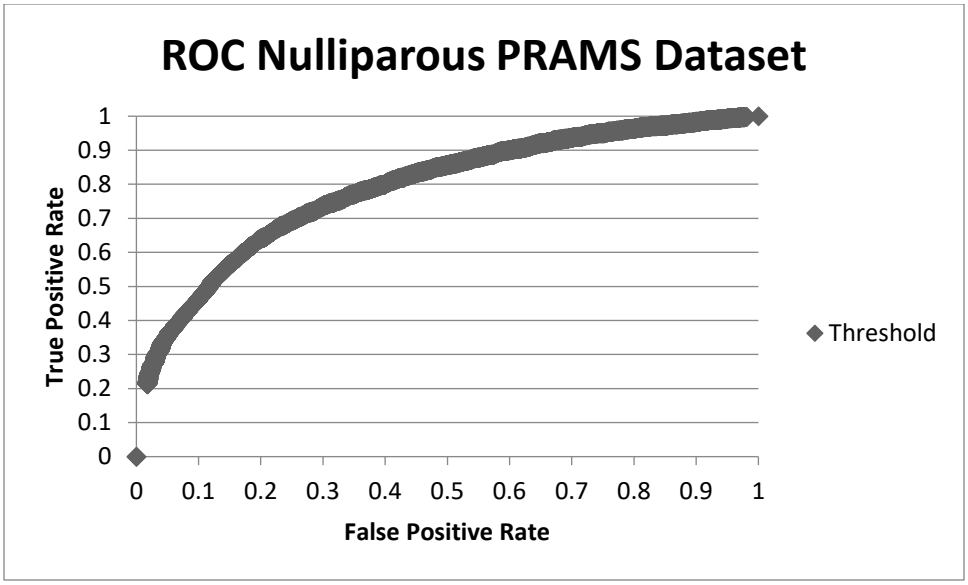
AUC: 0.888154

Figure 4.9. ROC Curve Performance for BORN Nulliparous Dataset



AUC: 0.805855

Figure 4.10. ROC Curve Performance for PRAMS Parous Dataset



AUC: 0.788409

Figure 4.11. ROC Curve Performance for PRAMS Nulliparous Dataset

The parameters of the best final networks, which optimize sensitivity, for the BORN and PRAMS Dataset at 7.9% Prevalence can be found in Appendix C. The final results of this research are summarized below in Tables 4.28-4.31.

4.9.Comparison to Past Results

Table 4.28. Display of the Artificial Neural Network results for BORN and PRAMS datasets

Datasets	Current Research (2018)		
	Sensitivity	Specificity	AUC
PRAMS_Parous	84.1%	71.4%	0.8059
PRAMS_Nulliparous	83.8%	76.0%	0.7884
BORN_Parous	89.2%	67.8%	0.8944
BORN_Nulliparous	89.0%	71.5%	0.8882

Table 4.29. Displays the Artificial Neural Network results for past results (2015)

Datasets	**Past Research** [24]		
	Sensitivity	Specificity	AUC
PRAMS_Parous	68.15%	64.17%	0.7256
PRAMS_Nulliparous	40.35%	94.75%	0.7064
BORN_Parous	50.53%	91.61%	0.7721
BORN_Nulliparous	53.96%	95.40%	0.7970

Table 4.30. Displays the Artificial Neural Network results for past results (2009)

Datasets	**Past Research** [27]		
	Sensitivity	Specificity	AUC
PRAMS_Parous	65.13%	84.07%	0.8195
PRAMS_Nulliparous	61.08%	71.14%	0.7195

Table 4.31. Displays the Artificial Neural Network results for past results (2007)

Datasets	**Past Research** [39]	
	Sensitivity	Specificity
PRAMS	65%	84%

4.10. Results and Discussion Summary

This research focused on data preparation methods in comparison to past research which focused on the machine learning algorithms. The first step dealt with class imbalance (ubBalance [76]) reducing the dataset from 679,697 (BORN) and 109,079 (PRAMS) cases to 102,187 (BORN) and 46,867 (PRAMS) cases. This was a major change from past research [24], [27], [11], and resulted in faster computational time building the ANN models and improved accuracy of the classifier during training and testing. In addition, the second step of filling in missing values using a package in R (missForest [48]), proved faster than a case-based reasoning approach to fill in missing values. Ong remarked difficulty with comparing past results with her current methodology, due to a variety of changes: a new ANN tool, introducing 5-by-2 cross validation to reduce bias of results, prevalence to simulate real world conditions and the use of an updated version of the PRAMS database. Therefore, effectiveness of these two data preparation methods were reflected in the improved sensitivity results, when following the methodology of Ong [24] closely. In addition, this research used significantly fewer variables (17-22) than past research (34-45 for Ong [24] and 48 for Catley [39]). This addressed an area of improvement discussed by Ong, who suggested fewer variables might result in better results.

There were promising results when evaluating the BORN and PRAMS dataset. Out of all the datasets, the BORN_Parous dataset had the best results when considering classifier performance (AUC) and sensitivity values. The Parous datasets had higher sensitivity metrics in comparison to the Nulliparous datasets, these datasets contain features with prior medical history (i.e. previous premature birth) and this seems to have a positive affect on the classifier's ability to classify preterm birth. There was an overall increase in sensitivity when comparing to past

results: 68.15% [24], 65% [27], 65% [39], meaning there are more accurate predictions when predicting preterm birth. Since, the objective of the thesis is to obtain the most accurate results when it comes to predicting preterm births, the specificity value is also important when referring to clinical costs and resources; however, it is not as critical as correctly predicting a premature birth outcome.

The aim was to exceed past sensitivity results and compare results to past performance metrics. The performance of the BORN and PRAMS database using the ANN Builder, did exceed past sensitivity results of prior students but did not surpass previous specificity metrics for all four datasets. One of the advantages of the ANN builder is its ability to optimize sensitivity or specificity; therefore, the model could be tailored specifically to fit the physician's needs, depending on which performance metric is desired. To be considered clinically useful in the context of this research a sensitivity of 65% and a specificity of 85% was recommended by our clinical partner [39], [24]. The sensitivity metric has been met and surpassed by all four datasets and future work will consist of improving the specificity metric to meet the clinical standards.

This chapter outlined the results obtained with this research work. The results of the methodology which focused on data preparation methods, showed an overall improvement in the sensitivity results of the Artificial Neural Network classifier. The reduced feature subsets for each of the four datasets were presented using the C5.0 DT Classifier. In addition, the performance metrics of the ANN classifier were displayed and compared to past work done in the MIRG lab. The contribution of this thesis work and future areas of improvement are discussed in the next chapter.

5. Chapter: Conclusion

5.1 Final Remarks and Conclusion

This thesis work was focused on improving the sensitivity results of predicting a preterm birth outcome using existing machine learning tools, applied to two large population-based datasets. The method of improving the sensitivity results focused on preprocessing methods, primarily addressing missing values and class imbalances found in the clinical datasets. In addition, with the use of the C5.0 DT classifier, similar important features were identified between these widely different datasets. This is a positive result as it shows some congruence between various databases; these features will be necessary to include when implementing a similar database system in a clinical environment. By addressing these common data preprocessing concerns, this thesis work contributed to a higher accuracy and faster computational time when generating the ANN models.

5.2 Contributions to Knowledge

1. This work demonstrated that the predictive system described in this thesis could potentially be used in both an American (PRAMS) and a Canadian environment (BORN). This provides further evidence that this algorithm could be further developed to someday be incorporated into obstetrical clinics in Canada where prenatal data is collected prospectively.
2. New tools were used in this research work: R, (missForest and ubBalance) and Tableau which have not been used previously by students in the MIRG lab for data preprocessing methods. Using R for imputing missing values has greatly improved computational time,

in comparison to previous methods (k-NN Algorithm). Tableau was an effective tool to visualize real-world data. In addition, this tool provided insight into the importance of some features over others, even before feature selection methods were applied. R and Tableau were chosen over other software tools such as SAS because these software tools needed to be open source to allow functionality within a clinical environment.

3. Similarly to previous students' work, the ANN classifier performed better with the BORN data than the PRAMS data [26], [29]. This may indicate that the variables collected by BORN may be more helpful to predict preterm births.
4. Previous work highlighted a need to attempt to reduce the number of variables used. This work has greatly reduced the number of features analyzed in the BORN (20 features for Parous and 17 features for Nulliparous) and PRAMS (22 features for Parous and 19 features for Nulliparous) in comparison to past work by Ong [24]: BORN (45 features for Parous and 38 features for Nulliparous) and PRAMS (48 features for Parous and 32 features for Nulliparous). This reduced feature subset maintained high sensitivity with reduced computational time.
5. These data preprocessing steps can be applied to variety of fields outside of the clinical sphere such as financial or environmental datasets with missing values; this is because these libraries in R are not specific to clinical data, are open-source and can handle large datasets.
6. Through data preprocessing methods described in the thesis, the sensitivity metric has surpassed previous methods, critical for predicting preterm births effectively; and the specificity metric has also remained sufficiently high. During the testing stage the

prevalence was set to 7.9%, to ensure that the data reflected an accurate population of preterm to term cases.

7. This work identified several similar features chosen by the DT classifier between both the PRAMS and BORN dataset:
    a. Multiple gestation
    b. Premature rupture of membranes
    c. Small gestation age
    d. Large gestational age
    e. Mother's age in years
    f. Number of previous preterm babies
    g. Hypertension
    h. Obstetrical complications (yes or no?)

These features might be important to maintaining high sensitivity results when moving the system to a real clinical environment.

8. During the feature selection methods, there were several features in the BORN dataset which were restricted from access due to data privacy concerns, such as geographical data; access to this data could result in an even higher sensitivity and specificity results for the classifier. As well as including shared features between BORN and PRAMS such as features including: hypertension, multiple gestation and maternal age. Given that the plan is to eventually integrate this classifier into a clinical environment in Canada, access to this data would be a great resource for future work. One option would be to anonymize the data so that researchers would have access to important information while still upholding the privacy of patients

9. This developed system is non-invasive and has the capability to predict a preterm birth prior to 23 weeks, using only data; it surpasses the accuracy of the current gold standard-fetal fibronectin.

5.3 Future Work

1. Future work should focus on improving the specificity performance metric (specifically dealing with the high number of false positives). There is an important trade-off between a high sensitivity and a high specificity. Although this work surpassed previous sensitivity results, the same was not true for the specificity metric. Specificity results were generally higher across the PRAMS datasets in comparison to BORN, therefore, certain features in PRAMS, were likely central to an increase in the specificity results. However, the specificity metric did not meet the clinical standard of 85%. Including similar features to those reported in the PRAMS dataset might be a solution to increasing this specificity metric.
2. Future work will include testing and validating the results from the use of these data preprocessing software. Data will be removed and then added back into the dataset, to test the validity of using the missForest package in R for imputing missing values. Similarly, for ubUnder this can be tested by removing different percentages of the data (using this package left 50% preterm and 50% term cases in the dataset) to ensure this 50% split between preterm and term cases represents the highest accuracy for predicting preterm birth; further work can be tested by observing how 60% preterm and 40% term cases affects the overall accuracy.
3. Future works consist of building a dataset of clinical features collected at obstetrical clinics from past neonatal cases with known labels of preterm or term cases. To build this

dataset, the similar features identified between the BORN and PRAMS dataset could be used to ensure high accuracy of the ANN classifier. Therefore, with future cases which contain unlabeled data, physicians will be able to make an accurate prediction on whether an individual may be at risk for a premature birth before 23 weeks gestation and then apply preventative care.

4. Investigate the effect of increasing the size of the testing set and see how the classifier performs. The classifier was tested in the final stage with 9210 term and 790 preterm cases from the BORN dataset. This testing set should be increased to test the stability of the performance of the classifier, with the same ratio between term and preterm cases. This can be done by randomly resampling the original 10,000 test set for an increased test set and then applying the classifier.
5. Eventually there will be a need to implement this system nationwide if it performs well in local clinics. Therefore, greater insight is needed into how this classifier will perform with data from populations in Canada, which have higher than normal preterm birth rates (rural and remote areas).
6. Future work could include integrating this predictive tool at a clinical site in conjunction with the prospective collection of data inputted into the Ontario Perinatal Record [37], through a secure web service. Preterm birth predictions made by the system could then be compared to the eventual pregnancy outcome, to determine the real-world accuracy of the prediction tool.

References

[1]		H. C. Koh and G. Tan, "Data mining applications in healthcare," Journal of healthcare information management, vol. 19, no 2, pp. 65-71, 2011.
[2]		J. Engel, "GE, IBM Race to Deliver on A.I. Hype in Healthcare," Xconomy Boston , 26 June 2017. [Online]. Available: https://www.xconomy.com/boston/2017/06/26/ge-ibm-race-to-deliver-on-a-i-hype-in-healthcare/. [Accessed 2018].
[3]		S. Armstrong, "The computer will assess you now," BMJ, London, vol. 355, no. 1, pp. 5680, 2016.
[4]		BORN, "BORN Information System," Better Outcomes and Registry & Network, 2013. [Online]. Available: https://www.bornontario.ca/en/born-information-system/. [Accessed 2017].
[5]		CDC, "Premature Birth," Center for Disease Control and Prevention, 2014. [Online]. Available: https://www.cdc.gov/prams/questionnaire.htm. [Accessed 2017].
[6]		J. R. Quinlan, " C5. 0 Data Mining Tool. RuleQuest Research.," 1997. [Online]. Available: https://www.rulequest.com/see5-info.html [Accessed 2017].
[7]		S. Nissen, "Implementation of a fast artificial neural network library (fann)," Department of Computer Science University of Copenhagen, Copenhagen, pp.1-92, 2003.
[8]		J. Wang, "Data mining: opportunities and challenges,". IGI Global, pp. 85-105, 2003.
[9]		N. Zhang and W. F. Lu, "An efficient data preprocessing method for mining customer survey data," Industrial Informatics, 2007 5th IEEE International Conference, vol. 1, pp. 573-578, 2007.
[10]		S. García, J. Luengo and F. Herrera, "Data preprocessing in data mining," Switzerland. Springer International Publishing, pp. 195-243, 2015.
[11]		C. Catley, M. Frize, R. C. Walker and D. C. Petriu, "Predicting high-risk preterm birth using artificial neural networks," IEEE transactions on information technology in biomedicine, vol. 10, no. 3, pp. 540-549, 2006.
[12]		M. Frize, N. Yu and S. Weyand, "Effectiveness of a hybrid pattern classifier for medical applications," International Journal of Hybrid Intelligent Systems, vol. 8, no. 2, pp. 71-79, 2011.
[13]		H. Martirosyan, M. Frize, D. E. Ong, J. Gilchrist and E. Bariciak, "A Decision-Support System for Expecting Mothers and Obstetricians," 6th European Conference of the International Federation for Medical and Biological Engineering. IFMBE Proceedings, vol. 45, pp. 703-706, 2015.
[14]		K. M. Groom and P. R. Bennett, "Tocolysis for the treatment of preterm labour-a clinically based review.," The Obstetrician & Gynaecologist, London, vol. 6, no. 1, pp. 4-11, 2004.
[15]		S. Beck, D. Wojdyla, L. Say, A. P. Betran, M. Merialdi, J. H. Requejo and P. F. Van Look, "The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity," Bulletin of the World Health Organization,vol. 88, pp. 31-38, 2010.
[16]		BORN Ontario, "Perinatal Health Indicators for Ontario 2012," 2012. [Online]. Available: https://www.bornontario.ca/assets/documents/specialreports/Perinatal%20Health%20Indicators%20for%20Ontario%202012.pdf.[Accessed 2018].
[17]		R. L. Goldenberg, J. F. Culhane, J. D. Iams and R. Romero, "Epidemiology and causes of preterm birth," The lancet, vol. 371, no. 9606, pp. 75-84, 2008.

[18]		S. A. Leonard, C. M. Crespi, D. C. Gee, Y. Zhu and S. E. Whaley, "Prepregnancy risk factors for preterm birth and the role of maternal nativity in a low-income, hispanic population.," Maternal and child health journal, vol. 19, no. 10, pp. 2295-2302, 2015.
[19]		P. J. Meis, R. L. Goldenberg, B. M. Mercer, J. D. Iams, A. H. Moawad, M. Miodovnik and A. Das, "The preterm prediction study: risk factors for indicated preterm births," American journal of obstetrics and gynecology, vol. 178, no. 3, pp. 562-567, 1998.
[20]		M. Parisaei, J. Currie, N. O'Gorman, S. Morris and A. L. David, "Implementation of foetal fibronectin testing: Admissions, maternal interventions and costs at 1 year," Journal of Obstetrics and Gynaecology, vol. 36, no. 7, pp. 888-892, 2016.
[21]		S. N. Deshpande, A. D. I. Van Asselt, F. Tomini, N. Armstrong, A. Allen, C. Noake and M. E. Westwood, "Rapid fetal fibronectin testing to predict preterm birth in women with symptoms of premature labour: a systematic review and cost analysis.," NIHR Journals Library, Southampton, vol. 40, no. 17, pp. 1-8, 2013.
[22]		N. L. Hezelgrave and A. H. Shennan, "Quantitative fetal fibronectin to predict spontaneous preterm birth: a review.," Women's Health, vol. 12, no. 1, pp. 121-128, 2016.
[23]		T. M. Malak, F. Sizmur, S. C. Bell and D. J. Taylor, "Fetal fibronectin in cervicovaginal secretions as a predictor of preterm birth," BJOG: An International Journal of Obstetrics & Gynaecology, vol. 103, no. 7, pp. 648-653, 1996.
[24]		D. E. Ong, "An Integrated Machine Learning Approach to Optimize the Estimation of Preterm Birth,". Carleton University, Ottawa, 2015.
[25]		PHIP, " Personal Health Information Protection Act,"November 2014 [Online]. Available: https://www.ontario.ca/laws/statute/04p03?search=phipa.[Accessed 2017].
[26]		T. M. Program, "BORN — Better Outcomes Registry and Network," 2013. [Online]. Available: https://www.themothersprogram.ca/resources-and-information/born-better-outcomes-registry-and-network.[Accessed 2018].
[27]		N. Yu, An integrated decision tree-artificial neural network hybrid to estimate clinical outcomes: ICU mortality and pre-term birth. Carleton University, Ottawa, 2009.
[28]		G. S. Berkowitz, C. Blackmore-Prince, R. H. Lapinski and D. A. Savitz, "Risk factors for preterm birth subtypes.," Epidemiology, vol. 9, no. 3, pp. 279-285, 1998.
[29]		P. J. Meis, R. L. Goldenberg, B. M. Mercer, J. D. Iams, A. H. Moawad, M. Miodovnik and A. Das, "The preterm prediction study: risk factors for indicated preterm births," American journal of obstetrics and gynecology, vol. 178, no. 3, pp. 562-567, 1998.
[30]		L. J. Muglia and M. Katz, "The enigma of spontaneous preterm birth," New England Journal of Medicine, vol. 362, no. 6, pp. 529-535, 2010.
[31]		G. Lim, J. Tracey, N. Boom, S. Karmakar, J. Wang, J. M. Berthelot and C. Heick, "CIHI survey: Hospital costs for preterm and small-for-gestational age babies in Canada," Healthcare Quarterly, vol. 12, no. 4, pp. 20-24, 2009.
[32]		S. Saigal and L. W. Doyle, "An overview of mortality and sequelae of preterm birth from infancy to adulthood," The Lancet, vol. 371, no. 9608, pp. 261-269, 2008.
[33]		T. Yoshizato, H. Obama, T. Nojiri, Y. Miyake, S. Miyamoto and T. Kawarabayashi, "Clinical significance of cervical length shortening before 31 weeks' gestation assessed by longitudinal observation using transvaginal ultrasonography," Journal of Obstetrics and Gynaecology Research, vol. 34, no. 5, pp. 805-811, 2008.
[34]		W. L. Maner, R. E. Garfield, H. Maul, G. Olson and G. Saade, "Predicting term and preterm delivery with transabdominal uterine electromyography.," Obstetrics & Gynecology,vol. 101, no.6, pp. 1254-1260, 2003.
[35]		H. Leitich and A. Kaider, "Fetal fibronectin—how useful is it in the prediction of preterm birth?," BJOG: An International Journal of Obstetrics & Gynaecology, vol. 110, no .20, pp. 66-70, 2003.

[36]		M. Frize, E. Bariciak, S. Dunn, S. Weyand, J. Gilchrist and S. Tozer, "Combined Physician-Parent Decision Support tool for the neonatal intensive care unit.," medical measurements and applications proceedings (MeMeA), vol. 197, pp. 59-64, 2011.
[37]		Provincial Council for Maternal and Child Health, "A User Guide to the Ontario Perinatal Record.," 2017. [Online]. Available: http://www.pcmch.on.ca/wp-content/uploads/2017/11/OPR_UserGuide_2017OCT26.pdf. [Accessed 2017].
[38]		P. H. Shiono and M. A. Klebanoff, "A review of risk scoring for preterm birth," Clinics in perinatology, vol. 20, no. 1, pp. 107-125, 1993.
[39]		C. Catley, An Integrated Hybrid Data Mining System for Preterm Birth Risk Assessment Based on a Semantic Web Servcies for Healthcare Framework, Carleton University, Ottawa, 2007.
[40]		J. R. Quinlan, "Bagging, boosting, and C4. 5.," AAAI/IAAI, vol. 1, pp. 725-730, 1996.
[41]		W. L. Maner and R. E. Garfield, "Identification of human term and preterm labor using artificial neural networks on uterine electromyography data," Annals of biomedical engineering, vol. 35, no. 3, pp. 465-473, 2007.
[42]		C. J. Lockwood and E. Kuczynski, "Risk stratification and pathological mechanisms in preterm delivery," Paediatric and perinatal epidemiology, vol. 15, pp. 78-89, 2001.
[43]		H. Y. Chen, C. H. Chuang, Y. J. Yang and T. P. Wu, "Exploring the risk factors of preterm birth using data mining.," Expert systems with applications, vol. 38, no. 5, pp. 5384-5387, 2011.
[44]		H. Kang, "The prevention and handling of the missing data," Korean journal of anesthesiology, vol. 64, no. 5, pp. 402-406, 2013.
[45]		G. Doquire and M. Verleysen, "Feature selection with missing data using mutual information estimators," Neurocomputing, vol. 90, pp. 3-11, 2012.
[46]		A. B. Pedersen, E. M. Mikkelsen, D. Cronin-Fenton, N. R. Kristensen, T. M. Pham, L. Pedersen and I. Petersen, "Missing data and multiple imputation in clinical epidemiological research," Clinical epidemiology, vol. 9, pp. 157-166, 2017.
[47]		A. K. Waljee, A. Mukherjee, A. G. Singal, Y. Zhang, J. Warren, U. Balis and P. D. Higgins, "Comparison of imputation methods for missing laboratory data in medicine," BMJ open, vol. 3, no. 8, pp.1-7, 2013.
[48]		D. J. Stekhoven and P. Bühlmann, "MissForest—non-parametric missing value imputation for mixed-type data.," Bioinformatics, vol. 28, no. 1, pp. 112-118, 2011.
[49]		S. V. Buuren and K. Groothuis-Oudshoorn, "mice: Multivariate imputation by chained equations in R," Journal of statistical software, vol. 10, no. 2, pp. 1-68, 2010.
[50]		M. J. Azur, E. A. Stuart, C. Frangakis and P. J. Leaf, "Multiple imputation by chained equations: what is it and how does it work?," International journal of methods in psychiatric research, vol. 20, no. 1, pp. 40-49, 2011.
[51]		J. A. Sterne, I. R. White, J. B. Carlin, M. Spratt, P. Royston, M. G. Kenward and J. R. Carpenter, "Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls," vol. 339, no. 7713, pp. 157-160, Bmj, 2009.
[52]		D. C. Li, C. W. Liu and S. C. Hu, "A learning method for the class imbalance problem with medical data sets.," Computers in biology and medicine, vol. 40, no. 5, pp. 509-518, 2010.
[53]		R. Longadge and S. Dongre, "Class imbalance problem in data mining review," vol. 2, no .1, pp. 1-6, 2013.
[54]		M. A. Mazurowski, P. A. Habas, J. M. Zurada, J. Y. Lo, J. A. Baker and G. D. Tourassi, "Training neural network classifiers for medical decision making: The effects of imbalanced datasets on classification performance," Neural networks,vol. 21, no. 2-3, pp. 427-436, 2008.
[55]		R. Longadge and S. Dongre, "Class imbalance problem in data mining review," International Journal of Computer Science and Network ,vol. 2, no.1, pp. 1-6, 2013.

[56]		M. M. Rahman and D. N. Davis, "Addressing the class imbalance problem in medical datasets.," International Journal of Machine Learning and Computing, vol. 3, no. 2, pp. 224, 2013.
[57]		V. Ganganwar, "An overview of classification algorithms for imbalanced datasets.," International Journal of Emerging Technology and Advanced Engineering, vol. 2. no. 4, pp. 42-47, 2012.
[58]		M. Vihinen, "How to evaluate performance of prediction methods? Measures and their interpretation in variation effect analysis," BMC genomics, vol 13. no. 4, pp. 1-10, 2012.
[59]		A. H. Fielding and J. F. Bell, "A review of methods for the assessment of prediction errors in conservation presence/absence models," Environmental conservation, vol. 24, no. 1, pp. 38-49, 1997.
[60]		J. Gilchrist, C. M. Ennett, M. Frize and E. Bariciak, "Neonatal mortality prediction using real-time medical measurements," medical measurements and applications proceedings (MeMeA), pp. 65-70, 2011.
[61]		B. Vidakovic, "Statistics for bioengineering sciences: with MATLAB and WinBUGS support," Springer Science & Business Media., pp. 471-472. 2011.
[62]		J. N. Mandrekar, "Receiver operating characteristic curve in diagnostic test assessment," Journal of Thoracic Oncology, vol. 5, no. 9, pp. 1315-1316, 2010.
[63]		S. Boughorbel, F. Jarray and M. El-Anbari, "Optimal classifier for imbalanced data using Matthews Correlation Coefficient metric," PloS one, vol 12. no. 6, pp.1-17, 2017.
[64]		MathWorks, "Normalize," R2015b. 2015 [Online]. Available: https://www.mathworks.com/help/matlab/ref/normalize.html#d119e785470.[Accessed 2017]
[65]		S. R. Maetschke, P. B. Madhamshettiwar, M. J. Davis and M. A. Ragan, "Supervised, semi-supervised and unsupervised inference of gene regulatory networks," Briefings in bioinformatics, vol. 15, no. 2, pp. 195-211, 2013.
[66]		S. B. Kotsiantis, I. Zaharakis and P. Pintelas, "Supervised machine learning: A review of classification techniques," Emerging artificial intelligence applications in computer engineering, vol. 160, pp. 3-24, 2007.
[67]		A. Abraham, F. Pedregosa, M. Eickenberg, P. Gervais, A. Mueller, J. Kossaifi and G. Varoquaux, "Machine learning for neuroimaging with scikit-learn," Frontiers in neuroinformatics, vol. 8, pp. 1-10, 2014.
[68]		Z. Ghahramani, "Unsupervised learning," Advanced lectures on machine learning , pp. 72-112, 2004.
[69]		J. H. Krijthe, "RSSL: Semi-supervised Learning in R," International Workshop on Reproducible Research in Pattern Recognition, pp. 104-115, 2016.
[70]		S. García, J. Luengo and F. Herrera, Data preprocessing in data mining, Granada: Springer International Publishing, pp. 195-243, 2015.
[71]		G. P. Zhang, "Neural networks for classification: a survey," IEEE Transactions on Systems, Man, and Cybernetics, Part C (Applications and Reviews), vol. 30, no. 4, pp. 451-462, 2000.
[72]		A. S. Galathiya, A. P. Ganatra and C. K. Bhensdadia, "Improved decision tree induction algorithm with feature selection, cross validation, model complexity and reduced error pruning.," International Journal of Computer Science and Information Technologies, vol. 3, no. 2, pp. 3427-3431, 2012.
[73]		I. G. Maglogiannis, Emerging artificial intelligence applications in computer engineering: real word ai systems with applications in ehealth, hci, information retrieval and pervasive technologies, Amsterdam: IOS Press, vol. 160, pp. 3-25, 2007.
[74]		R. Pandya and J. Pandya, "C5. 0 algorithm to improved decision tree with feature selection and reduced error pruning.," International Journal of Computer Applications, vol. 117, no. 16, pp. 18-21, 2015.

[75]		P. H. Swain and H. Hauska, "The decision tree classifier: Design and potential," IEEE Transactions on Geoscience Electronics, vol. 15, no. 3, pp. 142-147, 1977.
[76]		D. Pozzolo, O. Caelen and B. Gianluca, "Package 'unbalanced," 26 June 2015. [Online]. Available: https://cran.r-project.org/web/packages/unbalanced/unbalanced.pdf.[Accessed 2018].
[77]		M. Misztal, "Some Remarks on the Data Imputation Using "missForest" Method.,"pp. 1-11, 2013.
[78]		A. T. Azar, H. I. Elshazly, A. E. Hassanien and A. M. Elkorany, "A random forest classifier for lymph diseases.," Computer methods and programs in biomedicine, vol. 2, no. 113, pp. 465-473, 2014.
[79]		C. Nguyen, Y. Wang and H. N. Nguyen, "). Random forest classifier combined with feature selection for breast cancer diagnosis and prognostic," Journal of Biomedical Science and Engineering, vol. 5, no. 6, p. 551, 2013.
[80]		B. L. Kalman and S. C. Kwasny, "Why tanh: choosing a sigmoidal function," Neural Networks, vol. 4, pp. 578-581, 1992.
[81]		J. V. Tu, "Advantages and disadvantages of using artificial neural networks versus logistic regression for predicting medical outcomes," Journal of clinical epidemiology, vol. 11, no. 49, pp. 1225-1231, 1996.
[82]		Tableau, "Tableau Server 10.3.6," 12 December 2017. [Online]. Available: https://www.tableau.com/support/releases/server/10.3.6.[Accessed 2018].
[83]		Cygwin. [Online]. Available: https://www.cygwin.com/.[Accessed 2017].
[84]		J. R. Quinlan, "C5.0: An Informal Tutorial," RULEQUEST RESEARCH 2017, [Online]. Available: https://www.rulequest.com/see5-unix.html.[Accessed 2018].
[85]		C. M. Ennett, M. Frize and E. Charette, "Improvement and automation of artificial neural networks to estimate medical outcomes.," Medical engineering & physics, vol. 26, no. 4, pp. 321-328, 2004.
[86]		D. Rybchynski, "Design of an artificial neural network research framework to enhance the development of clinical prediction models," University of Ottawa, Ottawa, 2005.
[87]		A. S. Miller and B. H. Blott, "Review of neural network applications in medical imaging and signal processing.," Medical and Biological Engineering and Computing, vol. 30, no. 5, pp. 449-464, 1992.
[88]		J. Jiang, P. Trundle and J. Ren, "Medical image analysis with artificial neural networks," Computerized Medical Imaging and Graphics, vol. 34, no. 8, pp. 617-631, 2010.
[89]		S. A. Durai and E. A. Saro, "Image compression with back-propagation neural network using cumulative distribution function," World Academy of Science, Engineering and Technology, vol. 17, pp. 60-64, 2006.
[90]		M. Frize, J. Gilchrist, H. Martirosyan and E. Bariciak, "Integration of outcome estimations with a clinical decision support system: Application in the neonatal intensive care unit (NICU)," MeMeA, pp. 175-179, 2015.
[91]		J. Honaker, G. King, M. Blackwell and M. M. Blackwell, "Package 'Amelia'.," 2010. [Online]. Available: http://kambing.ui.ac.id/cran/web/packages/Amelia/Amelia.pdf.[Accessed 2018].

Appendices

Appendix A-Ethics Approval Form

Appendix B- Description of BORN and PRAMS Features

Appendix C- Description of ANN Final Network Parameters

Appendix A-Ethics Approval Form

External Researcher Data Sharing Agreement

CDC PRAMS AGREEMENT FOR SHARING MULTI-STATE DATA WITH EXTERNAL RESEARCHERS

I, Alana Esty, as principal investigator/coinvestigator on this proposed analysis of Pregnancy Risk Assessment Monitoring System (PRAMS) data, agree to the following requirements for the use of PRAMS data and assure compliance with the requirements by all staff and collaborators approved as part of this agreement.

1. I will not use these data except for statistical analysis and reporting as described in the attached proposal, titled Re-evaluating Perinatal Outcome Prediction Models Using Artificial Intelligence Tools and Recent Data from a Complex Perinatal Database, which accompanies this statement.
2. I will not use nor permit approved collaborators and staff to use these data to conduct analyses other than those described in the proposal.
3. I will not release the data set or any part of it to any person other than those listed as collaborators in the attached proposal. I will assure that all approved collaborators understand that they may not share the data set or any part of it.
4. I will neither attempt, nor permit others to attempt, to use the data set or link it with other data sets to learn the identity of any participant. If the identity of a respondent should be inadvertently discovered, I will not use and/or distribute this information, nor will I permit others to use the information. I will inform the CDC PRAMS staff at PRAMSProposals@cdc.gov of the discovery but will not disclose any identifiable data in the e-mail, so they can prevent future discoveries. I pledge that neither I nor other members of my team will inform anyone else of this knowledge.
5. All oral or written presentations of the results of the analyses will include an acknowledgment of the PRAMS Working Group and the Centers for Disease Control and Prevention (CDC).
6. All oral or written presentations of the results of the analyses will be submitted to the CDC at least 3 weeks prior to presentation or submission to a journal so presentations can be forwarded to the PRAMS participating states for their information. States will have two weeks to submit comments on the presentation/manuscript to the author. The acronym "PRAMS" will be submitted as a keyword for any publication.
7. CDC PRAMS staff and staff from states whose data were used in the analysis will be notified upon final publication of an article and provided with citation information.
8. When the proposed analyses are completed, all copies of these data will be destroyed (confirmed in writing to PRAMSProposals@cdc.gov) or returned to CDC.

My signature and the signatures of all co-investigators indicate our agreement to comply with these requirements.

Name of principal investigator: Dr. Erika Barrick

Title and Organization: CHILDREN'S Hospital of Eastern Ontario

Signature: [redacted] Date: Oct 19, 2016

Name of collaborator: Alana Esty

Signature: [redacted] Date: Oct. 19th, 2016

4

Appendix B – BORN and PRAMS Features

BORN Parous Features

1. MULTGEST	2. MATAGE
3. PPRETERM	4. PTERM
5. PARITY	6. PRESENT
7. DELTYPE	8. PREVCS
9. ANTESTER	10. GENDER
11. APGAR1	12. APGAR5
13. INTBF	14. SMOKING
15. MATHP0	16. MATHP1
17. MATHP2	18. MATHP3
19. MATHP4	20. MATHP5
21. MATHP16	22. MATHP17
23. MATHP18	24. MATHP19
25. MATHP26	26. MATHP27
27. OBCOMP0	28. OBCOMP1
29. OBCOMP2	30. OBCOMP3
31. OBCOMP4	32. OBCOMP5
33. OBCOMP6	34. OBCOMP7
35. OBCOMP8	36. OBCOMP9
37. OBCOMP10	38. OBCOMP11
39. OBCOMP12	40. OBCOMP13

41. OBCOMP14	42. OBCOMP15
43. REPASS	44. FIRSTVIS
45. CONGAN0	46. CONGAN52
47. CONGAN54	48. CONGAN55
49. DISCHTO	50. PRENCLAS
51. GBSRES	52. FISCALYEAR
53. LANGUAGE_up	54. MATHP_sub
55. MATHP_ment	56. CONGAN_CNS
57. CONGAN_EYE	58. CONGAN_OROFACIAL
59. CONGAN_CARDIAC	60. CONGAN_RES
61. CONGAN_GAS	62. CONGAN_GEN
63. CONGAN_MUS	64. CONGAN_CHR
65. Total_15_marital	66. Single
67. not_separated	68. separated
69. divorced	70. widowed
71. Total_15_common_law	72. Not_common_law
73. In_common_law	74. Total_families_1
75. Size_2_person	76. Size_3_person
77. Size_4_person	78. Size_5_or_more
79. Total_families_2	80. Total_couple_families
81. Married_couples	82. Without_children_at_home
83. With_children_at_home	84. child_1
85. children_2	86. children_3_over

87. Common_law_couples	88. Without_children_at_home1
89. With_children_at_home1	90. child1_1
91. children1_2	92. children1_3_over
93. Total_lone_parent_families	94. Female_parent
95. child2_1	96. children2_2
97. children2_3_over	98. Male_parent
99. child3_1	100. children3_2
101. children3_3_over	102. Average_number_children
103. Total_family_by_type	104. One_family
105. Multiple_family	106. Non_family
107. Total_by_mother_tongue	108. Single_responses
109. English	110. French
111. Non_official_languages	112. Total_by_immigrant
113. Non_immigrants	114. Immigrants
115. Total_by_Aboriginal	116. Total_Aboriginal
117. North_American_single	118. Metis_single_response
119. Inuit_single_response	120. Multiple_Aboriginal
121. Aboriginal_responses	122. Non_Aboriginal
123. Total_by_labour	124. In_labour_force
125. Employed	126. Unemployed
127. Not_in_labour_force	128. Total_by_class
129. Class_worker_NA	130. All_classes__worker
131. Paid_workers	132. Employees

133.	Self_employed	134.	Without_paid_help
135.	With_paid_help	136.	Self_employed_unco
137.	Without_paid_help2	138.	With_paid_help2
139.	Unpaid_family_workers	140.	Total_15_24_diploma
141.	No_diploma	142.	Certificate__diploma
143.	High_school	144.	Apprenticeship
145.	College__CEGEP_	146.	University_diploma
147.	diploma_or_below	148.	degree
149.	Bachelor_degree	150.	above_bachelor
151.	Degree_in_medicine	152.	Master_degree
153.	Doctorate	154.	Total_25_to_64_diploma
155.	No_diploma_degree	156.	Certi_diploma_degree
157.	High_school_certi	158.	Apprenticeship_diploma
159.	College_CEGEP_or_other	160.	University_dipoma
161.	diploma_below_bachelor	162.	University_certificate
163.	Bachelor_s_degree	164.	above_bachelor_degree
165.	Degree_medicine	166.	Master_s_degree
167.	Earned_doctorate	168.	Total_minority
169.	Total_visible_minority	170.	Total_by_ethnic
171.	British_Isles_origins	172.	French_origins
173.	Aboriginal_origins	174.	Other_American_origins
175.	Caribbean_origins	176.	Latin_Central
177.	European_origins	178.	African_origins

179.	Arab_origins	180.	West_Asian_origins
181.	South_Asian_origins	182.	East_Asian_origins
183.	Oceania_origins	184.	Family_income_2005
185.	Under_10_000	186.	IN_10_000_to_19_999
187.	IN_20_000_to_29_999	188.	IN_30_000_to_39_999
189.	IN_40_000_to_49_999	190.	IN_50_000_to_59_999
191.	IN_60_000_to_69_999	192.	IN_70_000_to_79_999
193.	IN_80_000_to_89_999	194.	IN_90_000_to_99_999
195.	IN_100_000_and_over	196.	Median_family_income
197.	Average_family_income	198.	Std_of_average_family
199.	Average_value_of_dwelling	200.	OUTCOME

BORN Nulliparous Features

1. MULTGEST	2. MATAGE
3. PARITY	4. PRESENT
5. DELTYPE	6. PREVCS
7. ANTESTER	8. GENDER
9. APGAR1	10. APGAR5
11. INTBF	12. SMOKING
13. MATHP0	14. MATHP1
15. MATHP2	16. MATHP3
17. MATHP4	18. MATHP5

19. MATHP16	20. MATHP17
21. MATHP18	22. MATHP19
23. MATHP26	24. MATHP27
25. OBCOMP0	26. OBCOMP1
27. OBCOMP2	28. OBCOMP3
29. OBCOMP4	30. OBCOMP5
31. OBCOMP6	32. OBCOMP7
33. OBCOMP8	34. OBCOMP9
35. OBCOMP10	36. OBCOMP11
37. OBCOMP12	38. OBCOMP13
39. OBCOMP14	40. OBCOMP15
41. REPASS	42. FIRSTVIS
43. CONGAN0	44. CONGAN52
45. CONGAN54	46. CONGAN55
47. DISCHTO	48. PRENCLAS
49. GBSRES	50. FISCALYEAR
51. LANGUAGE_up	52. MATHP_sub
53. MATHP_ment	54. CONGAN_CNS
55. CONGAN_EYE	56. CONGAN_OROFACIAL
57. CONGAN_CARDIAC	58. CONGAN_RES
59. CONGAN_GAS	60. CONGAN_GEN
61. CONGAN_MUS	62. CONGAN_CHR
63. Total_15_marital	64. Single

65. not_separated	66. separated
67. divorced	68. widowed
69. Total_15_common_law	70. Not_common_law
71. In_common_law	72. Total_families_1
73. Size_2_person	74. Size_3_person
75. Size_4_person	76. Size_5_or_more
77. Total_families_2	78. Total_couple_families
79. Married_couples	80. Without_children_at_home
81. Common_law_couples	82. Without_children_at_home1
83. Total_lone_parent_families	84. Female_parent
85. Male_parent	
86. Total_family_by_type	87. One_family
88. Multiple_family	89. Non_family
90. Total_by_mother_tongue	91. Single_responses
92. English	93. French
94. Non_official_languages	95. Total_by_immigrant
96. Non_immigrants	97. Immigrants
98. Total_by_Aboriginal	99. Total_Aboriginal
100. North_American_single	101. Metis_single_response
102. Inuit_single_response	103. Multiple_Aboriginal
104. Aboriginal_responses	105. Non_Aboriginal
106. Total_by_labour	107. In_labour_force
108. Employed	109. Unemployed

110.	Not_in_labour_force	111.	Total_by_class
112.	Class_worker_NA	113.	All_classes__worker
114.	Paid_workers	115.	Employees
116.	Self_employed	117.	Without_paid_help
118.	With_paid_help	119.	Self_employed_unco
120.	Without_paid_help2	121.	With_paid_help2
122.	Unpaid_family_workers	123.	Total_15_24_diploma
124.	No_diploma	125.	Certificate__diploma
126.	High_school	127.	Apprenticeship
128.	College__CEGEP_	129.	University_diploma
130.	diploma_or_below	131.	degree
132.	Bachelor_degree	133.	above_bachelor
134.	Degree_in_medicine	135.	Master_degree
136.	Doctorate	137.	Total_25_to_64_diploma
138.	No_diploma_degree	139.	Certi_diploma_degree
140.	High_school_certi	141.	Apprenticeship_diploma
142.	College_CEGEP_or_other	143.	University_dipoma
144.	diploma_below_bachelor	145.	University_certificate
146.	Bachelor_s_degree	147.	above_bachelor_degree
148.	Degree_medicine	149.	Master_s_degree
150.	Earned_doctorate	151.	Total_minority
152.	Total_visible_minority	153.	Total_by_ethnic
154.	British_Isles_origins	155.	French_origins

156.	Aboriginal_origins	157.	Other_American_origins
158.	Caribbean_origins	159.	Latin_Central
160.	European_origins	161.	African_origins
162.	Arab_origins	163.	West_Asian_origins
164.	South_Asian_origins	165.	East_Asian_origins
166.	Oceania_origins	167.	Family_income_2005
168.	Under_10_000	169.	IN_10_000_to_19_999
170.	IN_20_000_to_29_999	171.	IN_30_000_to_39_999
172.	IN_40_000_to_49_999	173.	IN_50_000_to_59_999
174.	IN_60_000_to_69_999	175.	IN_70_000_to_79_999
176.	IN_80_000_to_89_999	177.	IN_90_000_to_99_999
178.	IN_100_000_and_over	179.	Median_family_income
180.	Average_family_income	181.	Std_of_average_family
182.	Average_value_of_dwelling	183.	OUTCOME

PRAMS Parous Features

1. ID	2. B_ORDER
3. CIG_1TRI	4. CIG_2TRI
5. CIG_3TRI	6. CIG_PRIOR
7. DEFECT	8. FRACE_AMI
9. FRACE_ASN_NAPHSIS	10. FRACE_BLK

11. FRACE_CHN	12. FRACE_FLP
13. FRACE_JPN	14. FRACE_NHW
15. FRACE_WHT	16. HISP_BC
17. INFER_TR	18. KESSNER
19. LGA	20. MACROSOMIA
21. MARRIED	22. MAT_AGE_NAPHSIS
23. MAT_ED	24. MAT_RACE
25. MAT_TRAN	26. MAT_WIC
27. MM_DIAB	28. MM_FEVER
29. MM_HBP	30. MM_LMP
31. MM_NOMD	32. MM_PCV
33. MM_PROM	34. MOMCIG
35. MOMLBS	36. MOMSMOKE
37. MRACE_AMI	38. MRACE_ASN_NAPHSIS
39. MRACE_BLK	40. MRACE_CHN
41. MRACE_FLP	42. MRACE_JPN
43. MRACE_NHW	44. MRACE_OTH
45. MRACE_WHT	46. OTH_TERM
47. PAT_ED	48. PAY
49. PLURAL	50. PNC_MTH
51. PNC_VST_NAPHSI.S	52. PRE_LB_NAPHSIS
53. P_PRTERM	54. SEX
55. SGA_10	56. SGA_2SD

57. YY4_LMP	58. YY4_PCV
59. YY_LMP	60. HISPANIC
61. URB_RUR	62. BC_YRLLB
63. DRK63B_A	64. DRK63L_A
65. DRK6C_PG	66. INCOME5
67. MOM_BMI	68. MOM_BMIG
69. MOM_HT_I	70. MOM_WT
71. PNCNO	72. PNC_1TRM
73. PNC_WKS	74. PP_NUMB
75. PREGHX	76. SMK6C_PG
77. SMK6C_PP	78. STRS_TT3
79. STRS_T_G	80. SURE_WKS
81. OUTCOME	

PRAMS Nulliparous Features

1. ID	2. CIG_1TRI
3. CIG_2TRI	4. CIG_3TRI
5. CIG_PRIOR	6. DEFECT
7. FRACE_AMI	8. FRACE_ASN_NAPHSIS
9. FRACE_BLK	10. FRACE_CHN
11. FRACE_FLP	12. FRACE_JPN

13. FRACE_NHW	14. FRACE_WHT
15. HISP_BC	16. INFER_TR
17. KESSNER	18. LGA
19. MACROSOMIA	20. MARRIED
21. MAT_AGE_NAPHSIS	22. MAT_ED
23. MAT_RACE	24. MAT_TRAN
25. MAT_WIC	26. MM_DIAB
27. MM_FEVER	28. MM_HBP
29. MM_LMP	30. MM_NOMD
31. MM_PCV	32. MM_PROM
33. MOMCIG	34. MOMLBS
35. MOMSMOKE	36. MRACE_AMI
37. MRACE_ASN_NAPHSIS	38. MRACE_BLK
39. MRACE_CHN	40. MRACE_FLP
41. MRACE_JPN	42. MRACE_NHW
43. MRACE_OTH	44. MRACE_WHT
45. PAT_ED	46. PAY
47. PLURAL	48. PNC_MTH
49. PNC_VST_NAPHSI.S	50. SEX
51. SGA_10	52. SGA_2SD
53. YY4_LMP	54. YY4_PCV
55. YY_LMP	56. HISPANIC
57. URB_RUR	58. DRK63B_A

59. DRK63L_A	60. DRK6C_PG
61. INCOME5	62. MOM_BMI
63. MOM_BMIG	64. MOM_HT_I
65. MOM_WT	66. POB
67. PNCNO	68. PNC_1TRM
69. PNC_WKS	70. PP_NUMB
71. SMK6C_PG	72. SMK6C_PP
73. STRS_TT3	74. STRS_T_G
75. SURE_WKS	76. OUTCOME

Appendix C- Description of ANN Final Network Parameters

BORN Parous Method

FANN_FLO_2.1
num_layers=3
learning_rate=0.100000
connection_rate=0.100000
network_type=0
learning_momentum=0.000000
training_algorithm=3
train_error_function=0

train_stop_function=0
cascade_output_change_fraction=0.010000
quickprop_decay=-0.000100
quickprop_mu=1.750000
rprop_increase_factor=1.200000
rprop_decrease_factor=0.500000
rprop_delta_min=0.000000
rprop_delta_max=50.000000
rprop_delta_zero=0.100000
cascade_output_stagnation_epochs=12
cascade_candidate_change_fraction=0.010000
cascade_candidate_stagnation_epochs=12
cascade_max_out_epochs=150
cascade_min_out_epochs=50
cascade_max_cand_epochs=150
cascade_min_cand_epochs=50
cascade_num_candidate_groups=2
bit_fail_limit=3.49999994039535520000e-001
cascade_candidate_limit=1.0000000000000000000e+003
cascade_weight_multiplier=4.00000005960464480000e-001
cascade_activation_functions_count=10

cascade_activation_functions=3 5 7 8 10 11 14 15 16 17
cascade_activation_steepnesses_count=4
cascade_activation_steepnesses=2.50000000000000000000e-001 5.00000000000000000000e-001 7.50000000000000000000e-001 1.00000000000000000000e+000
layer_sizes=24 2 2
scale_included=0
neurons (num_inputs, activation_function, activation_steepness)=(0, 0, 0.00000000000000000000e+000) (24, 5,

5.000000000000000000e-001) (0, 5, 5.000000000000000000e-001) (2, 5, 5.000000000000000000e-001) (0, 5, 5.000000000000000000e-001)
connections (connected_to_neuron, weight)=(23, 1.25688269734382630000e-001) (0, 2.66311973333358760000e-001) (1, 6.09781086444854740000e-001) (2, 1.43165718764066700000e-002) (3, 4.80457663536071780000e-001) (4, 1.53704524040222170000e-001) (5, 3.56099337339401250000e-001) (6, -3.43392416834831240000e-002) (7, -1.38434067368507390000e-001) (8, 1.94338448345661160000e-002) (9, 8.59185308218002320000e-002) (10, 1.06069691479206090000e-001) (11, 6.98032155632972720000e-002) (12, 8.48777741193771360000e-002) (13, 3.99983779061585660000e-004) (14, 6.62460774183273320000e-002) (15, -1.86994001269340520000e-002) (16, 4.35047894716262820000e-002) (17, 8.23962539434432980000e-002) (18, -3.70812639594078060000e-002) (19, 3.71759310364723210000e-002) (20, 3.57275269925594330000e-002) (21, 5.73887117207050320000e-002) (22, -2.52741612493991850000e-002) (25, -7.18599511310458180000e-003) (24, -1.68719558715820310000e+001)

BORN Nulliparous Method

FANN_FLO_2.1
num_layers=3

learning_rate=0.900000
connection_rate=0.900000
network_type=0
learning_momentum=0.000000
training_algorithm=3
train_error_function=0
train_stop_function=0
cascade_output_change_fraction=0.010000
quickprop_decay=-0.000100
quickprop_mu=1.750000
rprop_increase_factor=1.200000
rprop_decrease_factor=0.500000
rprop_delta_min=0.000000
rprop_delta_max=50.000000
rprop_delta_zero=0.100000
cascade_output_stagnation_epochs=12
cascade_candidate_change_fraction=0.010000
cascade_candidate_stagnation_epochs=12
cascade_max_out_epochs=150
cascade_min_out_epochs=50
cascade_max_cand_epochs=150

cascade_min_cand_epochs=50
cascade_num_candidate_groups=2
bit_fail_limit=3.49999994039535520000e-001
cascade_candidate_limit=1.00000000000000000000e+003
cascade_weight_multiplier=4.00000005960464480000e-001
cascade_activation_functions_count=10
cascade_activation_functions=3 5 7 8 10 11 14 15 16 17
cascade_activation_steepnesses_count=4
cascade_activation_steepnesses=2.50000000000000000000e-001 5.00000000000000000000e-001 7.50000000000000000000e-001 1.00000000000000000000e+000
layer_sizes=22 2 2
scale_included=0
neurons (num_inputs, activation_function, activation_steepness)=(0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0,

0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (22, 13, 1.0000000149011612000e-001) (0, 13, 1.0000000149011612000e-001) (2, 13, 1.0000000149011612000e-001) (0, 13, 1.0000000149011612000e-001)
connections (connected_to_neuron, weight)=(21, -2.6702630519866943000e-001) (0, -8.5286331176757813000e-001) (1, -1.6895620822906494000e+000) (2, -5.9509035199880600000e-002) (3, -1.3281285762786865000e+000) (4, -5.0292742252349854000e-001) (5, -1.1362528800964355000e+000) (6, 1.1077578365802765000e-001) (7, 3.7108609080314636000e-001) (8, -7.6890297234058380000e-002) (9, -2.6142990589141846000e-001) (10, -3.4090071916580200000e-001) (11, -2.4585531651973724000e-001) (12, -3.0153635144233704000e-001) (13, -1.5097025781869888000e-002) (14, -1.5909136831760406000e-001) (15, -2.9550659656524658000e-001) (16, 8.5061989724636078000e-002) (17, -1.3574519753456116000e-001) (18, -9.5449239015579224000e-002) (19, -1.7135427892208099000e-001) (20, 7.7973119914531708000e-002) (23, -4.0841858834028244000e-002) (22, 9.5887245178222656000e+001)

PRAMS Parous Method

FANN_FLO_2.1
num_layers=3
learning_rate=0.100000
connection_rate=0.900000
network_type=0
learning_momentum=0.000000
training_algorithm=3
train_error_function=0
train_stop_function=0
cascade_output_change_fraction=0.010000
quickprop_decay=-0.000100
quickprop_mu=1.750000
rprop_increase_factor=1.200000
rprop_decrease_factor=0.500000
rprop_delta_min=0.000000
rprop_delta_max=50.000000
rprop_delta_zero=0.100000
cascade_output_stagnation_epochs=12
cascade_candidate_change_fraction=0.010000

cascade_candidate_stagnation_epochs=12
cascade_max_out_epochs=150
cascade_min_out_epochs=50
cascade_max_cand_epochs=150
cascade_min_cand_epochs=50
cascade_num_candidate_groups=2
bit_fail_limit=3.49999994039535520000e-001
cascade_candidate_limit=1.00000000000000000000e+003
cascade_weight_multiplier=4.00000005960464480000e-001
cascade_activation_functions_count=10
cascade_activation_functions=3 5 7 8 10 11 14 15 16 17
cascade_activation_steepnesses_count=4
cascade_activation_steepnesses=2.50000000000000000000e-001 5.00000000000000000000e-001 7.50000000000000000000e-001 1.00000000000000000000e+000
layer_sizes=22 2 2
scale_included=0
neurons (num_inputs, activation_function, activation_steepness)=(0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0,

0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (0, 0, 0.0000000000000000000e+000) (22, 13, 5.0000000000000000000e-001) (0, 13, 5.0000000000000000000e-001) (2, 13, 5.0000000000000000000e-001) (0, 13, 5.0000000000000000000e-001)
connections (connected_to_neuron, weight)=(21, -4.8162136226892471000e-003) (0, -3.7761837244033813000e-001) (1, 2.7132600545883179000e-001) (2, 2.0147739350795746000e-001) (3, 3.8923019170761108000e-001) (4, 1.8038573861122131000e-001) (5, 1.8196688592433929000e-001) (6, -6.7293673753738403000e-002) (7, 6.2691003084182739000e-002) (8, -1.0773003846406937000e-001) (9, -2.1676467359066010000e-001) (10, -2.8605191037058830000e-002) (11, -1.9271614030003548000e-002) (12, -3.6717176437377930000e-002) (13, 8.9186869561672211000e-002) (14, 6.2506131827831268000e-002) (15, 4.3230082839727402000e-002) (16, 4.1900862008333206000e-002) (17, -4.2947724461555481000e-002) (18, 1.5906054526567459000e-002) (19, 1.5051889419555664000e-001) (20, -

9.955771267414093000000e-002) (23, 2.021268159151077300000e-001) (22, -8.732421875000000000000e+000)

PRAMS Nulliparous Method

FANN_FLO_2.1
num_layers=3
learning_rate=0.100000
connection_rate=0.100000
network_type=0
learning_momentum=0.000000
training_algorithm=3
train_error_function=0
train_stop_function=0
cascade_output_change_fraction=0.010000
quickprop_decay=-0.000100
quickprop_mu=1.750000
rprop_increase_factor=1.200000
rprop_decrease_factor=0.500000
rprop_delta_min=0.000000

rprop_delta_max=50.000000
rprop_delta_zero=0.100000
cascade_output_stagnation_epochs=12
cascade_candidate_change_fraction=0.010000
cascade_candidate_stagnation_epochs=12
cascade_max_out_epochs=150
cascade_min_out_epochs=50
cascade_max_cand_epochs=150
cascade_min_cand_epochs=50
cascade_num_candidate_groups=2
bit_fail_limit=3.49999994039535520000e-001
cascade_candidate_limit=1.00000000000000000000e+003
cascade_weight_multiplier=4.00000005960464480000e-001
cascade_activation_functions_count=10
cascade_activation_functions=3 5 7 8 10 11 14 15 16 17
cascade_activation_steepnesses_count=4
cascade_activation_steepnesses=2.50000000000000000000e-001 5.00000000000000000000e-001 7.50000000000000000000e-001 1.00000000000000000000e+000
layer_sizes=20 2 2
scale_included=0

neurons (num_inputs, activation_function, activation_steepness)=(0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (0, 0, 0.00000000000000000000e+000) (20, 13, 5.00000000000000000000e-001) (0, 13, 5.00000000000000000000e-001) (2, 13, 5.00000000000000000000e-001) (0, 13, 5.00000000000000000000e-001)
connections (connected_to_neuron, weight)=(19, 1.87676306813955310000e-002) (0, 3.46589267253875730000e-001) (1, -2.97859013080596920000e-001) (2, -3.89916002750396730000e-001) (3, -2.26215943694114690000e-001) (4, 7.55250155925750730000e-002) (5, -1.93298980593681340000e-001) (6, 7.11965858936309810000e-002) (7, -1.62846028804779050000e-001) (8, 8.92773196101188660000e-002) (9, -3.60125824809074400000e-002) (10, 7.41084944456815720000e-003) (11, -7.02089443802833560000e-002) (12, 1.44820913672447200000e-001) (13, 2.34051253646612170000e-002) (14, -

7.2304837405681610000e-002) (15, -7.5000584125518799000e-002) (16, 4.4615093618631363000e-002) (17, 8.2279061898589134000e-003) (18, -2.5776792317628860000e-002) (21, -3.7022095173597336000e-002) (20, 8.2015094757080078000e+000)