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Maternal Nutritional Factors Enhance Birthweight Prediction: A Super Learner Ensemble Approach

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Abstract: Birthweight (BW) is a widely used indicator of neonatal health, with low birthweight (LBW) being linked to higher risks of morbidity and mortality. Timely and precise prediction of LBW is crucial for ensuring newborn health and well-being. Despite recent machine learning advancements in BW classification based on physiological traits in the mother and ultrasound outcomes, maternal status in essential micronutrients for fetal development is yet to be fully exploited for BW prediction. This study aims to evaluate the impact of maternal nutritional factors, specifically mid-pregnancy plasma concentrations of vitamin B12, folate, and anemia on BW prediction. This study analyzed data from 729 pregnant women in Tarragona, Spain, for early BW prediction and analyzed each factor's impact and contribution using a partial dependency plot and feature importance. Using a super learner ensemble method with tenfold cross-validation, the model achieved a prediction accuracy of 96.19% and an AUC-ROC of 0.96, outperforming single-model approaches. Vitamin B12 and folate status were identified as significant predictors, underscoring their importance in reducing LBW risk. The findings highlight the critical role of maternal nutritional factors in BW prediction and suggest that monitoring vitamin B12 and folate levels during pregnancy could enhance prenatal care and mitigate neonatal complications associated with LBW.

Keywords: birthweight prediction; ensemble learning; machine learning; super learner; maternal nutrients

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1. Introduction

Birthweight (BW) is the most critical marker of neonatal health. It influences health and survival, and its early prediction would assist medical professionals in making timely decisions. A BW of fewer than 2500 g is classified as low birthweight (LBW) [1]. Numerous factors, such as metabolic anomalies, short interpregnancy intervals, maternal malnutrition, low socioeconomic status, high parity, and infections contribute to LBW [2]. Significant metabolic and physiological transformations occur during pregnancy, increasing the mother's caloric and nutritional requirements to support fetal growth and maternal health [3]. Suboptimal maternal nutritional status has been strongly associated with adverse birth outcomes, including LBW, which can have long-term consequences on the offspring's development and health [4]. These include cognitive disorders, hearing loss, neonatal hypoglycemia, cardiovascular disease, diabetes, and premature death [5,6]. The World Health Organization (WHO) highlighted LBW as a significant health issue in 2019, affecting more than 20 million neonates in 2015, which is approximately one in seven births globally. Of the 2.5 million neonates that die annually worldwide, over 80% of these have LBW [7]. Adequate maternal nutrient status, both while planning and during pregnancy, is essential for optimal BW in the offspring [8]. It is also crucial to understand the influence of maternal nutrients on birth outcomes, especially LBW, to prevent adverse birth outcomes.

The developing fetus relies entirely on maternal intake and stores of essential nutrients throughout pregnancy. Notably, maternal status in vitamin B12, folate, and anemia are closely linked to birth outcomes and fetal growth. Insufficient status can result in limited nutrient availability to the fetus, leading to poor fetal development [9–11]. Low maternal vitamin B12 status is associated with a higher risk of preterm birth, LBW, and cognitive disorders in the offspring [12]. Adequate folate status is required during pregnancy for rapid cell proliferation, fetal growth, and increased maternal blood volume [13]. Furthermore, anemia during pregnancy is a global public health concern because it causes premature birth and consequently LBW [14].

Underlying factors leading to physiological changes during pregnancy such as fetal sex, gestational age (GA), gestational diabetes mellitus (GDM), and lifestyle factors, such as smoking, all influence BW. BW is higher in males than in females because male fetuses and embryos need more calories due to their higher metabolic rate [15]. Medical professionals schedule prenatal screenings and evaluations according to the gestational age of the fetus. BWs at either end of the scale, such as large for gestational age (LGA) and small for gestational age (SGA), are risk factors for neonatal illness and morbidity [16]. GDM is the first occurrence of elevated blood glucose after 20 gestational weeks (GWs), after which placental function is fully established, and recent studies widely accept that macrosomia or high gestational age at delivery are the most common adverse pregnancy outcome affected by GDM [17].

In addition, smoking during pregnancy has been widely recognized as a significant adverse factor on BW. Maternal smoking exposes the developing fetus to harmful chemicals, including nicotine and carbon monoxide, which can impair fetal growth and development [18]. Studies have consistently shown that maternal smoking is associated with a higher likelihood of LBW in the neonate [19]. The detrimental impact of smoking on BW can be attributed to several factors, including reduced oxygen supply to the fetus, constriction of blood vessels in the placenta, and potential disruptions in maternal–fetal nutrient transport. Smoking during pregnancy has also been linked to preterm birth and an increased risk of various neonatal complications [20]. Consequently, reducing maternal smoking is essential to improve BW and promote overall maternal and fetal health during pregnancy.

The accurate early prediction of BW has long been a priority for obstetricians and clinical researchers. Various studies have explored its prediction and assessment using a range of clinical attributes, including maternal age, height, ultrasound measurements of the fetus (such as abdominal circumference, head circumference, biparietal diameter), and maternal body mass index (BMI) [21,22]. Surprisingly, despite the acknowledged importance and association of maternal nutrients with BW, there is a notable absence of publications combining maternal nutritional status with machine learning (ML) for BW prediction. Given its potential significance in predicting neonatal BW, further investigation is warranted to determine the extent of their influence and their integration into ML predictive models.

ML techniques are useful tools that medical practitioners can consider using in various healthcare applications, including BW classification and estimation. ML models offer the potential to unravel the influence of maternal nutrient status on BW prediction and study their intricate associations with BW [23]. Furthermore, ML algorithms can unveil hidden patterns within datasets and eliminate redundant or extraneous information, thereby revealing significant correlations or dependencies in the existing data. However, the utilization of ML algorithms in medical applications presents its own set of challenges. These are due to the stringent requirement for high-quality data in training and testing ML-based systems, and medical datasets are often affected by missing records that can affect the performance of ML-based systems [24].

Consequently, this work addresses the challenges of achieving better performance and results from ML models for BW prediction. To enhance ML results, we explore the potential benefits of an ensemble learning approach, which combines multiple single models to improve prediction performance and generalizability [25]. The main objective of this study is to identify the most suitable ensemble learning algorithm, including single-base models and the super learner (SL) model, and determine the optimal combination of single-base models for predicting BW class (LBW or normal BW (NBW)). We aim to investigate the contributions and effects not only of commonly used factors such as fetal sex, GDM, GA at the time of blood draw, and smoking but also maternal nutritional factors, such as vitamin B12 and folate status and anemia. Our findings, derived from the SL and single-base models, shed light on the critical role of important clinical factors associated with adverse pregnancy outcomes and inadequate BW (<2500 g). To the best of our knowledge, this is the first study to use ML models and an ensemble learning for BW prediction, incorporating a diverse range of clinical nutritional factors, such as maternal vitamin B12, folate, and anaemia, as well as common physiological and lifestyle factors such as fetal sex, GDM, GA and smoking. The data for all of these attributes were collected between 24 and 27 GWs. Consequently, the main contributions of this work are as follows:

1. Innovative Birth Cohort Analysis: Introduction of the first machine learning-based analysis for BW prediction, conducted within the Reus–Tarragona Birth cohort from University Hospitals Sant Joan, Reus, and Joan XXIII, Tarragona, Spain. The research leverages an original dataset encompassing physiological, lifestyle, and nutritional features from 729 pregnant women in the Tarragona region, Spain, to effectively determine neonatal BW. The evaluation results of the SL model are further utilized for BW classification.
2. Exploration of Maternal Nutritional Influence: Novel exploration into the influence of maternal nutrient status, specifically plasma vitamin B12, folate, and anaemia, on neonatal BW prediction using the SL model, representing an innovative and previously unexplored area of research.
3. Comprehensive Feature Analysis: Utilization of seven critical physiological, lifestyle, and nutritional features (including fetal sex, GA, GDM, smoking, vitamin B12, folate, and anemia) in multiple experiments. This study evaluates the performance of four individual models: Extra Trees (ETs), Random Forest (RF), AdaBoost, and LightGBM) as base learners, alongside an assessment of the SL model.
4. Optimized Model Integration: Introduction of a novel combination of base learners to achieve optimal performance in BW prediction using the SL approach.
5. Insightful Feature Assessment: Utilization of Gini importance scores to quantify the impact of each feature on the overall predictive model, offering valuable insights into their relative significance.
6. Detailed Feature Analysis: Utilization of Partial Dependency Plots to visually illustrate and comprehend how physiological, lifestyle (e.g., smoking), and nutritional features influence BW, thereby providing deeper insight into the relationships between specific features and the model's predictions.

The remainder of the paper is organized as follows: The literature review is reported in Section 2. The dataset and study design details are described in Section 3. The proposed ML models are explained in Section 4. The experimental findings and results are reported in Section 5, and the conclusion and suggested future work are summarized in Section 6.

2. Related Work

2.1. ML for Predicting Birthweight

Previous research has predominantly focused on physiological factors and sometimes lifestyle attributes for BW classification or estimation using advanced ML models, such as Decision Tree (DT), Artificial Neural Network (ANN), RF, Support Vector Machine (SVM) and Logistic Regression (LR) (see Table 1). Table 1 provides an overview of the existing

BW classification and BW estimation literature. The table outlines the cohorts and factor categories analysed, along with the ML models employed and their respective outcomes.

Table 1. Summary of BW Classification related work.

Literature	Cohort	Factors	Goal	ML Models	Results
Arayeshgari et al., 2023 [21]	741 pregnant women from Fatemieh hospital, Iran	Clinical data from physiological factors	Prediction of LBW	DT, ANN, RF, SVM and LR for LBW classification	LR outperformed with sensitivity and specificity of 0.74 ± 0.09 and 0.89 ± 0.03
Feng et al., 2019 [26]	7875 pregnant women registered in West China Secondary Hospital	Clinical data from Physiological and Ultrasound characteristics	Fetal weight estimation	DBN for fetal weight estimation and SVM for classification	DBN achieved MAE of 198.55 ± 158 g and SVM achieved MAPE of 6.09 ± 5.06%
Wasif Khan et al., 2022 [22]	821 women in the United Arab Emirates (UAE) hospital	Dataset consists of Physiological and Lifestyle factors	LBW prediction and BW estimation	LR and RF for Regression and Classification	MAE of 294.53 g is achieved by RF and LR achieved best accuracy of 90.24%
Faruk et al., 2018 [27]	12,055 pregnant women registered in IDHS	Physiological and Lifestyle factors	Predicting LBW	LR and RF for BW classification	RF outperformed LR with 93% accuracy
Hussain et al., 2020 [28]	445 pregnant women from Assam health centre, India	Clinical data from physiological factors	Prediction of LBW	Gaussian NB and RF for BW classification	RF achieved accuracy of 100% with recall and F1 score of 1.0
Trujillo et al., 2020 [29]	250 pregnant women from National Institute of Perinatology, Mexico	Clinical data from Physiological and Ultrasound characteristics	Estimation of BW	SVR for regression task	MPE of 0.364 ± 11.95% and an MAE of 287.60 ± 195.86 g is achieved by SVR
Senthilkumar et al., 2015 [30]	189 mothers recruited by Baystate Medical Center Massachusetts	Study included Physiological and Lifestyle factors	Prediction of LBW	CT, NB, LR, ANN, RF and SVM for BW classification	CT achieved the best accuracy of 0.899, AUC of 0.72
Borson et al., 2020 [31]	4498 mothers record from Bangladeshi Demographic and Health Survey	Study included Physiological and Lifestyle factors	Prediction of LBW	MLP, SVM NB, LR and KNN for classification of BW	SVM outperformed other models with accuracy of 80.29%
Kumar et al., 2020 [32]	175 pregnant women recruited by Assam Medical College in India	Dataset consists of sociologic and polycyclic features	Prediction of LBW	NB, SVM and AdaBoost for BW classification	SVM achieved an accuracy of 81.21%, sensitivity and specificity of 0.84 and 0.74
Yarlapati et al., 2017 [33]	101 pregnant women records from Indian Health Camps	Study included demographic features	Early LBW prediction	Bayes minimum error rate for classification	Bayes minimum error rate achieved an accuracy of 96.77%

Table 1. *Cont.*

Literature	Cohort	Factors	Goal	ML Models	Results
Loreto et al., 2019 [34]	2328 pregnant women from Portuguese hospital	Study included Physiological and Lifestyle factors	Prediction of LBW	AdaBoost, Tree, RF, KNN, NB and SVM for classification	AdaBoost outperformed with accuracy of 98%, sensitivity of 0.91, and specificity of 0.99
Akbulut et al., 2018 [35]	Turkish RadyoEmar Imaging Center recruited 96 pregnant women	Dataset consists of physiological and lifestyle factors	Fetal Health Status	AP, DF, BDT, BPM, NN, LR, and SVM for BW classification	DF outperformed with accuracy of 89.5%

For instance, Arayeshgari et al. [21] compared the performance of five ML algorithms, i.e., DT, ANN, RF, SVM and LR, in the prediction of LBW. The results highlighted LR's superior performance over the other ML models, attributing the prediction success to maternal age, neonatal sex, gestational age, parity, number of previous miscarriages, and hereditary factors as the most influential maternal factors associated with LBW. While the study effectively predicted BW and identified the crucial features, the disparity in feature scaling could potentially affect the attributes' importance score. Feng et al. [26] reported an SVM-based BW classification and deep belief network (DBN) based model for fetal weight estimation, including maternal and ultrasound parameters. The research demonstrated promising outcomes in BW classification and estimation. However, the study's complex methodology resulted in high computational demands and reduced processing speed. Wasif Khan et al. [22] used and evaluated thirty ML algorithms to estimate BW and classify LBW using a physiological and lifestyle features dataset. LR and RF achieved the best results from the thirty ML models. The study emphasized the significance of hypertension, GA, and GDM in BW classification. However, the study had limitations regarding accurate BW estimation, as indicated by a notably high mean absolute error, and struggled with issues of model overfitting. Faruk et al. [27] used RF and LR algorithms for LBW classification and prediction on physiological and lifestyle factors based on a dataset collected from women aged 15 to 49. The results indicated RF's superior performance over LR in classification and prediction tasks. However, the study's findings were limited due to unsatisfactory results, with an AUC score of 0.505, indicating a deficient discriminatory power that could lead to biased and inaccurate model predictions. Hussain et al. [28] proposed the Gaussian Naive Bayes (GNB) and RF models to classify BW on the physiological feature-based dataset. The findings indicated that RF outperformed GNB in terms of performance. However, the study revealed potential issues with biased ML models, and an increase in the number of trees led to reduced processing speed, thereby affecting the model's efficiency. Trujillo et al. [29] employed the SVM to estimate the neonate BW using physiological and ultrasound features collected during the 1st trimester of pregnancy. While the study's approach was relatively straightforward to understand, the research demonstrated limitations in performance, evidenced by a high mean absolute error and a notable reliance on high memory usage, which could impede practical application and scalability.

Additionally, Senthilkumar et al. [30] carried out a performance comparison of six different ML models LR, Naive Bayes (NB), SVM, ANN, classification tree (CT) and RF for LBW prediction using the dataset of physiological and lifestyle features. The findings highlighted the superior performance of the CT model compared with the other ML approaches. However, the study indicated a crucial need for more data to facilitate enhanced generalization, as the current limitations could lead to overfitting and model instability. Borson et al. [31] used six ML models including LR, NB, KNN, RF, SVM and MLP for BW classification, using a dataset containing ten features based on physiological and lifestyle factors. The results indicated the superior performance of the SVM over the other ML models. However, the study highlighted a limitation concerning the need for a more comprehensive description of the dataset, which could potentially lead to misinterpretation of the data and its implications. Kumar et al. [32] used NB, AdaBoost and SVM models to predict neonate LBW from a dataset of 120 women who gave birth to NBW neonates and 55 mothers of LBW neonates, using sociodemographic and polycyclic aromatic hydrocarbon features. The results indicated that SVM was superior to the other ML models. However, the study's reliance on a relatively small dataset limited its representativeness of the overall population scenario, resulting in potential overfitting issues and model instability. Yarlapati et al. [33] developed a screening tool to classify normal and LBW to assist medical professionals using the Bayes minimum-error-rate classifier in a dataset of 18 significant demographic features. The ML model used achieved an excellent accuracy score, highlighting the pivotal role of maternal age, weight, and community status as the most influential factors in classifying BW. However, the small dataset of just 101 women was a limitation of the study and led to unstable testing and validation results, model overfitting and reduced complexity. Loreto et al. [34] proposed six ML models, i.e., KNN, DT, AdaBoost, RF, SVM and NB, for BW classification on datasets containing physiological and lifestyle features. The authors tested the prediction of LBW under various combinations of features to determine their respective impacts. They found that the combination encompassing all features yielded the most significant effect and performance, mainly when using the AdaBoost model. However, the study indicated extended model training time and high memory usage as potential challenges associated with the proposed approach. Akbulut et al. [35] reported an ML-based intelligent medical system to predict fetal anomalies in a mother- child dyads dataset containing physiological and lifestyle features. The findings revealed that the decision forest model outperformed other ML models and emphasized the significance of fetal age, maternal age, and blood serotype as crucial features. However, the study's reliance on a relatively small dataset limited its representativeness of a broader population, highlighting the need for additional data to train a stable ML model.

Thus, ML and associated techniques are being increasingly used in predicting BW. These studies underscore the significance of reasonable ML algorithm selection, handling class imbalances, and accounting for crucial maternal and neonatal factors. While the reviewed papers offer valuable insights into BW prediction using ML and related techniques, they have overlooked the influence of maternal nutritional factors on BW prediction. While these studies primarily focus on physiological and lifestyle factors such as maternal age, neonatal sex, GA, and smoking, our research emphasizes that maternal nutritional elements such as vitamin B12 and folate, as well as hemoglobin status are significantly associated with BW. Therefore, future studies could comprehensively investigate these nutritional factors and their integration into predictive models.

2.2. Nutrition Impact on BW

Optimal maternal nutrition significantly influences maternal and neonatal survival, as well as women's overall health, well-being, and daily activities. Over 3 million annual neonatal deaths are linked to undernutrition, and the primary cause of death is LBW and preterm birth [36]. Recent clinical studies and shreds of evidence show that maternal vitamin B12, plasma folate, and anemia are significantly associated with BW in their offspring [9–11].

In a systematic review, Behere et al. [37] report that low maternal vitamin B12 status is associated with offspring outcomes. The observational studies support the associations of low maternal vitamin B12 status with neural tube defects (6 studies), pregnancy complications such as pre-eclampsia and recurrent pregnancy loss (9 studies), LBW (10 studies), and adverse short-long term health outcomes in the offspring (11 studies).

Yuan et al. [38] investigated the association between maternal vitamin B12 and folate status and adverse pregnancy outcomes in a cohort study of 11,549 women using general linear regression models. They observed a significant association between vitamin B12 and folate status and adverse pregnancy outcomes, including LBW. The authors found that low folate status was strongly associated with pre-eclampsia (PE) and intrahepatic cholestasis of pregnancy (ICP). Higher vitamin B12 status was linked with a higher risk of ICP, PE, large for gestational age (LGA) neonates, and GDM, whereas lower vitamin B12 status was associated with decreased BW, a low probability of having an LGA neonate, and a high risk of pregnancy-induced hypertension.

Furthermore, Finkelstein et al. [39] examined anemia prevalence and its association with neonate outcomes and adverse pregnancy outcomes in a study of 366 pregnant women. Binomial and linear regression models were used to assess the association between maternal anemia biomarkers, adverse pregnancy, and newborn outcomes. Thirty percent of the women were anemic and associated with a higher risk of premature birth and LBW.

The compelling evidence from the studies discussed above highlights the potential of maternal status in vitamin B12, folate, and anemia as valuable predictors of neonatal BW. This study classified BW with input and guidance from healthcare experts and obstetricians. This classification serves a dual purpose: Firstly, it facilitates the identification of specific risk factors associated with different BW classes, such as LBW, which can encompass factors like premature birth, socioeconomic conditions, and maternal health. Healthcare practitioners can leverage this information to enhance maternal and neonatal outcomes by identifying and addressing these risk factors. Secondly, our research and public health professionals can use BW classification to analyze patterns and trends in BW across diverse populations. This analysis is instrumental in understanding the prevalence of LBW among babies in particular regions, shedding light on health inequalities and disparities. Such insights are invaluable for developing effective public health policies and initiatives to improve neonatal health outcomes and address inequalities in BW.

3. Materials

Two datasets were used in this study: a private dataset from the Reus–Tarragona birth cohort and the publicly accessible IEEE Child Birth Weight dataset referenced in [40].

3.1. Reus–Tarragona Cohort

3.1.1. Study Participants and Data Collection

The Reus–Tarragona birth cohort study is a prospective study from early pregnancy throughout childhood carried out by the Unit of Preventive Medicine and Public Health, Faculty of Medicine and Health Sciences of the Universitat Rovira i Virgili (URV) in collaboration with the Departments of Obstetrics and Gynaecology in the university hospitals: Sant Joan, Reus and Joan XXIII, Tarragona (registered at https://clinicaltrials.gov/; NCT01778205 accessed on 22 October 2022). The data used for this study are from the pregnancy phase of the study. Pregnant women were invited to participate in this study based on the following criteria.

Inclusion criteria: Women with a confirmed singleton pregnancy and viable fetus that were less than 12 weeks pregnant at their first prenatal blood draw were eligible to participate.

Exclusion criteria: Use of medication affecting folate or cobalamin status, chronic diseases, or surgical operations that influence nutritional status or habits, as well as multiple pregnancies.

There were 45 miscarriages among the 831 pregnant women who accepted the invitation and participated in the study. A total of 57 out of the remaining 786 pregnancies were not followed to completion because of stillbirth, termination due to fetal abnormality, transfer to another hospital, or loss to follow-up for unknown reasons. Seven hundred twenty-nine mothers with corresponding neonatal BW were included in this analysis. Biochemical determinations from fasting blood samples obtained in EDTA- K3 tubes [41] between 24 and 27 GWs were used for this study. Blood collection time was recorded, and the samples were kept refrigerated before sample processing for nutrient determinations (plasma folate and vitamin B12, and hemoglobin), which was carried out in less than an hour.

Data regarding GA, plasma folate, vitamin B12, anemia, smoking, and GDM were obtained from the prenatal clinical records at the time point of 24–27 GWs. Maternal plasma folate and vitamin B12 status were determined by microbiological assays using *Lactobacillus casei* [42] and *Lactobacillus leichmannii* [43], respectively. Women's anemia status was assessed by blood hemoglobin concentration (<10.5 g/dL). BW was recorded by trained personnel using a standard beam balance at birth. The seven clinical features, i.e., fetal sex, GA, vitamin B12, plasma folate, mid-pregnancy anemia, and GDM versus none, were included as predictors of BW in this study's outcome. These features were selected based on previous evidence associating them with BW [9–11].

3.1.2. Characteristics of Collected Data

The upper part of Table 2 summarizes the characteristics of the clinical features used in this study with their mean, standard deviation (SD), maximum, and minimum. The correlation heatmap displaying the relationships between maternal attributes and their correlations with neonatal BW collected from the Reus-Tarragona cohort provided in the Supplementary Material. Figure 1 shows the distribution and interpretation of the overall collected data; of 729 live births, 365 newborns were boys, and 364 were girls. Of 729 neonates, 53 had LBW, and 676 had NBW. According to the non-pregnant reference ranges of plasma vitamin B12, 543 of 729 women had sufficient plasma vitamin B12 status (>221 nmol/L), 155 had insufficient status (≥148 nmol/L to ≤221 nmol/L), and 31 were deficient (<148 pmol/L). Plasma vitamin B12 sufficiency indicates adequate vitamin B12 status to maintain health; a low status indicates a status lower than that necessary to maintain a healthy life, and deficiency indicates that the body lacks plasma vitamin B12 to function correctly. Additionally, plasma folate status was deficient (<7 nmol/L) in 123 mothers. As pregnancy progresses, a woman's vitamin B12 and folate status declines. So, the reference values used above are based on data from adults (men and non-pregnant women). The means (SD) of maternal plasma vitamin B12 and folate concentrations were 292.3 (101.8) pmol/L and 19.9 (17.0) nmol/L, respectively. The mean GA at 24–27 GWs blood draw was 24.3 ± 1.5 weeks. Forty-seven women had GDM confirmed by elevated blood glucose during the glucose tolerance test, and thirty mothers were found to be anemic at 24–27 GWs. Of 729 pregnant women, 530 never smoked during the pregnancy, 79 only smoked during the 1st trimester, and 120 smoked throughout the pregnancy.

This study leverages the above physiological, lifestyle, and nutritional features to assess their significance as neonatal BW predictors. Previous studies have identified these factors as direct or indirect critical contributors to LBW. Physiological determinants, such as preterm birth (before 37 GWs) and preeclampsia, are strongly associated with LBW [44,45]. Lifestyle factors, particularly maternal smoking, are associated with impaired placental efficiency, leading to reduced BW [46]. Additionally, nutritional imbalances, often linked to impaired cellular proliferation and intrauterine growth restriction, further contribute to LBW outcomes in neonates [12,13,47].

Table 2. Feature information of Reus–Tarragona and IEEE birth cohort dataset.

Attribute	Description	Min	Max	Mean	SD
	Reus Tarragona Birth Cohort				
Sex	Newborn sex	0	1	-	-
GA	Gestational age during 2nd trimester	11	28	23	1.8
Vitamin B12	2nd trimester plasma Vitamin B12 concentration (pmol/L)	80.8	815.4	292.3	101.8
GDM	First occurrence of diabetes after 20 GW	0	1	-	-
Anemia	Hemoglobin ≤ 10.5 dg/L at 24–27 GWs	0	1	-	-
Folate	2nd trimester Plasma Folate concentration (nmol/L)	3.2	131.4	19.9	17.0
Smoking	Smoking pattern of mother during pregnancy	0	2	-	-

Table 2. *Cont.*

Attribute	Description	Min	Max	Mean	SD
	IEEE Child Dataset				
Age	Age of the newborn's mother	16	38	22	4.28
Height	Height of the mother (cm)	120	195	142	17.24
Blood group	Mother's blood group	0	7	-	-
Pregnancy history	Number of pregnancies in the past	0	4	-	-
Sex	Newborn sex	0	1	-	-
Initial systolic BP	Mother's initial systolic blood pressure (mmHg)	70	150	105.9	22.23
Initial diastolic BP	Mother's initial diastolic blood pressure (mmHg)	50	90	65.89	7.7
Final systolic BP	Mother's final systolic blood pressure (mmHg)	80	150	111.10	13.11
Final diastolic BP	Mother's final diastolic blood pressure (mmHg)	50	100	70.61	8.57
Initial hemoglobin	Mother's initial hemoglobin level (g/dL)	8	12.2	10	1.05
Final hemoglobin	Mother's final hemoglobin level (g/dL)	7.5	13.2	10.45	0.96
Blood sugar	Mother's blood sugar level (mg/dL)	59	159	100.66	11.48
Socioeconomic	Parents socioeconomic status	0	1	-	-

3.2. IEEE Birth Cohort

The IEEE dataset comprises 1215 records and 13 features derived from clinical data of pregnant women in Assam, India. Data collection followed a systematic and professionally supervised process, ensuring no variables were arbitrarily selected. Medical professionals carefully curated the dataset, incorporating clinically relevant features recognized as critical for health evaluations. The selection of these features adheres to established medical guidelines, enhancing the dataset's robustness and suitability for clinical research [48]. The lower part of Table 2 reports the features used in this dataset and offers a statistical description of each maternal feature. The dataset encompasses a range of demographic, physiological, nutritional, and lifestyle maternal features, including maternal age, height, blood group, and comprehensive blood pressure measurements recorded at various stages of pregnancy. Key features such as fetal sex, initial and final hemoglobin levels, and blood sugar status are included due to their established influence on birth outcomes, particularly BW. Recent studies, referenced in [48,49], also thoroughly explain the publicly available IEEE childbirth dataset.

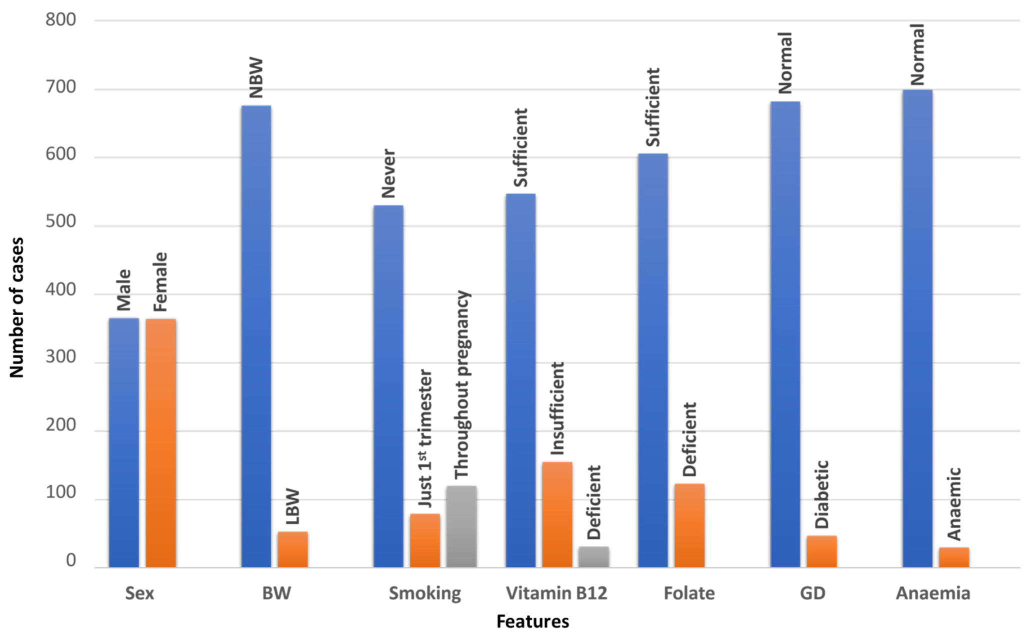

Figure 1. Bar chart for neonate gender (sex), BW and mother's smoking pattern during pregnancy, maternal vitamin B12 status, maternal plasma folate status, gestational diabetes mellitus, maternal anemia.

4. Methods

The flow chart and architectural view of the proposed approach adopted in the current study are shown in Figure 2, which illustrates that the dataset was created with seven different features, which consist of three physiological features (fetal sex, GDM, and GA), three nutritional features (maternal status in vitamin B12, folate, and anemia), and one lifestyle feature (smoking). Missing values in the medical dataset are a major problem affecting machine learning models' learning rate, performance, and clinical decision-making [50]. We deal with this problem by first excluding any clinical feature with missing values of 40% or more, and second, by imputing the missing values using linear interpolation (LI) [51] when they affect less than 40% of the clinical feature. The outliers were removed to prepare the dataset for ML models. The dataset was normalized to keep the data on the same scale and obtain the best performance of ML models. Another problem we faced in the dataset was BW class imbalance. The latest class balancing variant, Instance Weighted Synthetic Minority Oversampling Technique (IW-SMOTE) [52], was applied to the training dataset. The well-processed dataset was split into training and testing sets to train and test the SL model. As shown in Figure 2, single-based (level 0) and meta-learner (level 1) algorithms make up the SL model, and this section introduces the basic concept behind the SL model. These particular ML techniques in the SL model were chosen because they are generally accepted, reasonably explain the dependent variable, and work admirably with a limited amount of data [53]. A feature importance score and partial dependency plot of each feature were used to assess each clinical feature's importance and impact, especially the nutritional factors in predicting BW. Finally, the results of the proposed ML models and SL model were evaluated and analyzed using a variety of performance measures.

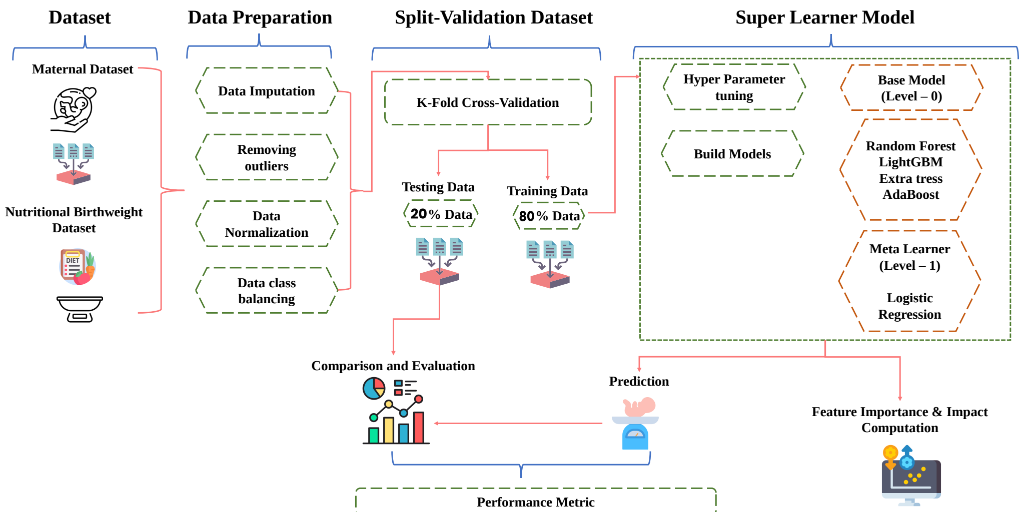

Figure 2. The proposed approach for this study.

4.1. Data Preprocessing

The combination of physiological, nutritional, and lifestyle data was used as the main dataset for training our ML models. Data preprocessing is necessary to correctly explore the influence of each clinical feature on BW and achieve good predicting performance. In this study, the data were prepared using different data preprocessing techniques.

4.1.1. Data Imputation

The clinical data were collected in the first, second, and third trimesters of pregnancy. The collected data had missing values, as expected, because this is typical in medical datasets. Due to the dataset's time series collection and structure, the LI technique was used to estimate the missing values because of its accepted performance in estimating missing values in time series data. LI uses the nearest one or two data points to infer the missing values, and it does this by connecting the closest points in a straight line. The missing values in clinical features at 24–27 GAs were estimated using the mother's first and third trimester data with the help of LI. The LI formula is

$$\hat{y} = y_1 + (x - x_1)\,\frac{(y_2 - y_1)}{(x_2 - x_1)}, \tag{1}$$

where x_1 and y_1 are the first coordinates, x_2 and y_2 are the second coordinates, x is the point to perform the interpolation, and $\hat{y}$ is the interpolated value.

4.1.2. Removing Outliers

Outliers in the dataset were addressed using the Interquartile Range (IQR) [54] method. This standard technique identified and removed unusual data points that significantly differed from other observations. Specifically, seven outliers were removed from the "vitamin B12" and "folate" features. These outliers were considered to be of unusual status compared with the rest of the data. Other features and labels did not have outliers as they consist of categorical values, which inherently limit the occurrence of such anomalies.

4.1.3. Data Normalization

Data normalization is an essential part of data preprocessing in machine learning. It ensures the efficient training of models, maintenance of numerical stability, and equal importance distributed to all features by keeping the data on the same scale. ML models usually show acceptable performance when data are normalized [55]. Data normalization was essential to achieve the main objectives of this study, as it helped to obtain better performance in predicting the BW class by improving the convergence of optimization algorithms, ensuring that each feature is contributing equally to the model learning process, preventing overfitting of ML models, and also helping to facilitate the calculation of clinical feature impact, especially nutritional status, on the models by providing better interpretability of model feature importance or coefficients. We scale the data from 0 to 1 using the MinMax scaler (MMS) [56] normalization technique. The MMS formula is

$$\hat{x} = \frac{x - min(x)}{max(x) - min(x)}, \tag{2}$$

where x is the input data, and $\hat{x}$ is the normaliszed data.

The experimental results showed that data normalization improved the accuracy of the ML models.

4.1.4. Data Balance

Class imbalance in our dataset is another major issue because it significantly reduces ML model or classification system performance. Instances of LBW (Minority class) were relatively infrequent, likely because the data were obtained in a developed country. Therefore, most instances were biased in favor of the NBW (Majority class), and the leading causes from our and previous studies [57] were the established healthcare system and reasonable annual income. Due to class imbalance, the classification system ignores the minority class (LBW) and leads the results towards the majority class (NBW). In our training dataset, the majority class (NBW) had 545 instances, and the minority class (LBW) had only 32 cases. In the past, this problem has been solved by undersampling the majority class and oversampling the minority class by duplicating the randomly chosen samples. A well-known data balancing technique called the instance-weighted synthetic minority oversampling technique (IW-SMOTE) oversamples the minority class by generating synthesized samples and keeping a similar data distribution with a slight difference from the original data [22]. In this study, IW-SMOTE is applied to the ML model's training data to address the problem of class imbalance and no artificial or duplicate data were used in the test data. Table 3 shows the number of instances in majority and minority classes before and after implementing IW-SMOTE to overcome the biasing of the classification system towards NBW.

Table 3. Number of instances in each class before and after IW-SMOTE.

Before IW-SMOTE		After IW-SMOTE	
Class	**Instances**	**Class**	**Instances**
Majority class (NBW, 0)	545	Majority class (NBW, 0)	545
Minority class (LBW, 1)	32	Minority class (LBW, 1)	545

4.2. Split-Validation of the Dataset

In this study, we used the nested cross-validation (CV) technique to improve model accuracy and precision. Of 729 cases, 80% were used to train the models and 20% to test them based on the hold-out technique. While splitting the dataset, we used stratified sampling to ensure that the testing and training sets have roughly the same number of outcomes or target values. The K-fold cross-validation approach was utilized to train the set to obtain optimal results. Usually, a k value of 5 or 10 is used because allocating the immense value increases the computational cost. A tenfold CV was used in this study on the training dataset.

4.3. Proposed Super Learner Approach

As shown in Figure 2, the SL model section illustrates the structure of this proposed approach. This approach consists of base-learners (level 0), meta-learner (level 1), and hyperparameter tuning. The Python library ML-Ensembles was used to implement the SL model, and Jupiter Notebook was used as a development environment.

4.3.1. Super Learner Model

The term "super learner model (SL)" does not refer to a specific machine learning model; rather, it represents an ensemble learning technique known for its ability to combine multiple base learning algorithms to yield a more accurate and robust predictive model [58,59]. The core idea behind SL modeling is to leverage the diversity of different models to enhance predictive performance.

The SL model operates at two levels: level 0 and level 1. In level 0, several individual base ML models were trained on the provided training dataset. Each base model is tasked with learning patterns and relationships within the data. level 1, conversely, comprises meta-learners trained on the predictions generated by the base learners using a cross-validation (CV) technique. CV is an integral component as it helps assess the performance of the entire ensemble.

Here is an overview of how the SL model works:

- The original dataset is partitioned into V blocks, each used to train an individual base model.
- Hyperparameter tuning is applied to each base model to optimize its performance.
- Predictions are generated by the base models using a k-fold cross-validation approach. Importantly, all predictions generated during the k-fold process are retained for subsequent use.
- The SL model is then fed with these predictions from the base models as input parameters. The meta-learner, operating at level 1, learns to combine these predictions effectively, leveraging the insights from the diverse base models. This allows the meta-learner to perform two crucial tasks simultaneously: learning the best combination of predictions and making predictions on unseen or new data. We keep all predictions that are out of k-fold. Later, they can use the model to make predictions in cases not present during training because each base model fits the whole training dataset.

Figure 3 visually represents the data flow within the proposed SL model, illustrating the relationships between the base models, predictions, and the meta-learner.

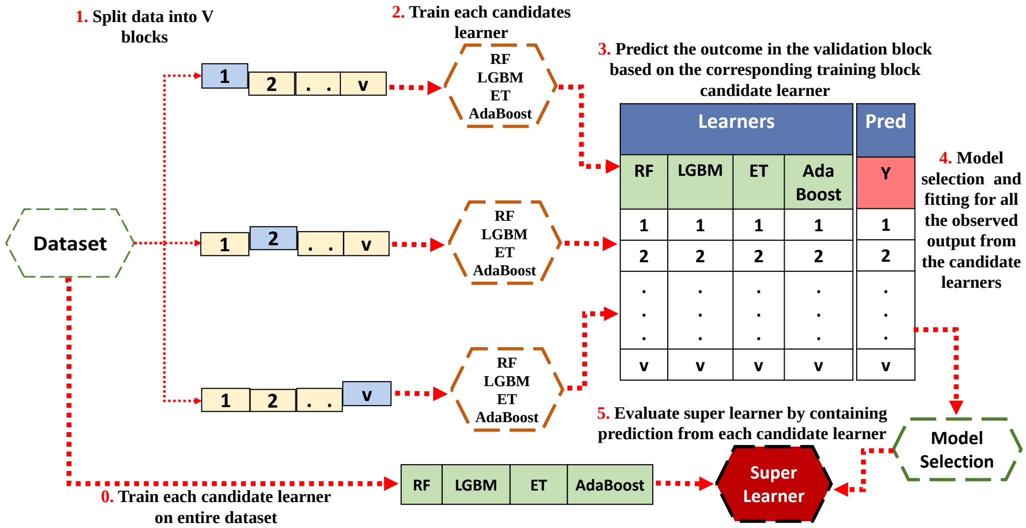

Figure 3. The data flow of the super learner model.

4.3.2. Case Studies for the Creation of the Super Learner Model

The main aim of this study is to develop a robust SL model for BW prediction. A comprehensive case study was conducted in constructing the proposed SL model to achieve this goal. Various ML techniques were harnessed in this process to create four distinct super-ensemble models. Single-based ML models were used at level 0 in the first SL model. For the second and third SL models, a combination of boosting and bagging ensemble learning techniques was applied at level 0. Finally, the fourth SL model was tailored by merging single-base, boosting, and bagging algorithms.

A separate case study was also conducted to identify the optimal meta-learner algorithm at level 1. Various ML algorithms, including KNN, LR, ANN, Bagging, and SVM, were rigorously assessed to determine the ideal meta-learner algorithm for the proposed SL model. The findings from this case study demonstrated that the fourth SL model, comprising level 0 models such as RF, LightGBM, ETs, and AdaBoost, coupled with a level 1 LR meta-learner, delivered the optimal performance. These case studies underscore the novelty of our research by showcasing the selection process for level 0 and level 1 algorithms within the SL framework.

4.3.3. Base Learner Algorithms (Level 0)

This section explains the single-based algorithms used in level 0 of the supermodel. RF, LightGBM, ETs, and AdaBoost were used as base models in level 0. These ML models have comprehensive utilization, efficient results in medical problems and showed good performance in the published studies discussed in the related work section. The rest of this section provides details about the selected base learners in level 0.

Random Forest (RF): The RF classifier is a member of the ensemble learning community, a popular ML algorithm. RF efficiently handles numerical and categorical data and is mainly used for classification problems. The RF classifier makes predictions based on the combination of multiple decision trees. Predictions are made by averaging the results of individual decision trees, and each is trained on a unique subset of training data [60]. We used the RF because of its ability to handle noisy datasets, high dimensional data, and feature interactions. It shows robustness and efficient performance with new and unseen data and provides valued insights into feature importance.

Light Gradient Boosting Machine (LightGBM): The LightGBM is a popular gradient-boosting frame for low or large-scale data due to its memory efficiency and speed. LightGBM was developed by Microsoft and based on the gradient boosting concept, in which a series of weak prediction models (usually decision trees) are trained to compensate for earlier models' errors to prepare a strong predictive model. The other gradient boosting frameworks, like XGBoost, employ the level-wise tree growth strategy, but LightGBM uses the leaf-wise tree growth strategy to lower the loss by growing the tree more efficiently. LightGBM combines two techniques, gradient-based on-side sampling (GOSS) and exclusive feature bundling (EFB), to optimize its training to be 20 times faster than other algorithms [61]. The speedier training time, low memory usage, and high accuracy on a limited dataset make it suitable for our study.

Extra Trees (ET): The ETs model is an ensemble ML algorithm and an extended version of the RF algorithm. It refers to the part of the decision-tree-based algorithms family. ETs is used for both classification and regression tasks. ETs performs bootstrap sampling, random feature selection, splitting and building trees, and aggregation of the prediction from each tree. The ETs help to reduce overfitting, increase diversity, reduce biasing among the trees, and speed up the training process [62].

AdaBoost: AdaBoost, also called Adaptive Boosting, is a powerful ML model primarily used for classification. AdaBoost's central principle is to prioritize difficult-to-classify data by making successive weak learners focus on the samples that were previously misclassified. AdaBoost's ability to boost weights adaptively means it can provide a robust classifier that works well across a wide range of decision boundary conditions. AdaBoost's effectiveness relies on the nature of the data and well-tuned hyperparameters. The key advantages of AdaBoost are high accuracy, versatility, and avoidance of overfitting [63].

4.3.4. Meta Learner Algorithm (Level 1)

The proposed SL approach employs LR as the meta-learner. LR is a well-established machine learning algorithm renowned for its effectiveness in predicting binary classes, such as yes or no, 0 or 1, in classification tasks. Despite its name, LR is not a regression technique but a classification algorithm. It leverages the logistic function, often called the sigmoid function, to model the relationship between input features and the likelihood of a specific outcome. This sigmoid function enables the estimation of probabilities, converting numerical inputs into values ranging between zero and one. LR boasts several notable advantages and characteristics, including simplicity, interpretability, efficiency, rapid processing, and a probabilistic interpretation [64].

4.3.5. Hyperparameter Tuning

The tuning of hyperparameters is crucial to implementing an ML model, as they determine how the learning algorithm operates. The model's performance, generalizability, and computing efficiency can all be significantly improved by tuning the hyperparameters to their optimal values. The grid search technique was used for hyperparameter tuning in the ML models used. Using a grid search, a range of values for each hyperparameter can be specified and then model performance across all ranges can be thoroughly tested. It can be beneficial when the hyperparameter space is manageable, and the number of hyperparameters is minimal. However, it can become computationally expensive for a high number of hyperparameters or a considerable range of values. It is noted that RF, LightGBM, ETs, and AdaBoost were used as base learners in creating the proposed super learner approach, and LR was used as a meta-learner. Table 4 shows the hyperparameters tuning values of the implemented ML models in predicting neonate BW.

Table 4. Hyperparameter tuning of the employed machine learning models.

Model	Parameter	Ranges	Optimal
RF	n_estimators max_depth criterion	10, 20, 50, 100, 200, 300, 400, 500 1, 3, 5, 7, 9, 11 'gini', 'entropy'	100 5 entropy
LightGBM	max_bin num_leaves learning_rate	1, 3, 5, 7, 9, 11 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0	7 30 0.2
ET	n_estimators criterion max_depth	10, 20, 50, 100, 200, 300, 400, 500 'gini', 'entropy' 1, 3, 5, 7, 9, 11, 13, 15, 17	150 gini 7
AdaBoost	learning_rate algorithm	0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0 'SAMME', 'SAMME.R'	0.3 SAMME
LR	C penalty	0.001, 0.01, 0.1, 1, 10, 100, 1000 L1, L2	1 L2

4.4. Evaluation Metrics

Evaluation metrics are crucial for measuring the effectiveness and performance of ML models. This study used the accuracy, precision, recall, F1 score, and ROC curves as evaluation metrics to compare the performance of single-based algorithms and ensemble learning models. It is essential to use the *ROC* curves because of the class imbalance nature of the data. The formulas of the above-mentioned evaluation metrics are as follows:

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN}, \tag{3}$$

$$Precision = \frac{TP}{TP + FP}, \tag{4}$$

$$Recall = \frac{TP}{TP + FN}, \tag{5}$$

$$F1 = \frac{2 * Precision * Recall}{Precision + Recall}, \tag{6}$$

$$ROC = \frac{TPR}{FPR}, TPR = \frac{TP}{TP + FN}, FPR = \frac{FP}{FP + TN}, \tag{7}$$

where true positive (*TP*) is the number of neonates with true positive BW in the model; true negative (*TN*) is the number of neonates with true-negative BW in the model; false positive (*FP*) is the number of neonates with false-positive BW in the model; and false negative (*FN*) is the number of neonates with false-negative BW in the model. AUC's highest and lowest values, representing the area under the *ROC*, are 1 and 0. The AUC value closest to 1 is considered the optimal value.

4.5. Feature Importance Computation

In ML, the relative significance of various features is calculated using the feature importance technique. It helps identify each feature's impact on the outcome or model's predictor. This technique is used in this study to determine the effect of commonly used physiological clinical features, i.e., fetal sex, GDM, GA, and nutritional clinical features, i.e., plasma folate, vitamin B12, anemia, and lifestyle features, i.e., smoking, in the prediction of BW class by the above-discussed machine learning algorithms.

Tree-based ML models selected in this study, such as the Random Forest, Extra Trees, LightGBM, and Adaboost algorithms, provide built-in mechanisms to determine feature importance. The feature importance score of the ML models used is calculated by the Gini Importance method (also known as mean decrease impurity) [65]. Across the entire model's tree distribution, it quantifies how each feature decreased the impurity criterion (usually Gini impurity or entropy). Features are considered more important and highly reduce the impurity when used for splitting. The importance score is calculated across the tree in an ensemble by averaging the importance score. The increment in leaf purity increases the feature's importance.

5. Experiments

The experiment was conducted using the approach described above. The SL model was implemented in Python (Python version 3.10) and executed on Jupyter Notebook. The scikit-learn library was used for predictive analysis, and tenfold cross-validation was applied to optimize results. Performance was evaluated using accuracy, precision, recall, and F1 score metrics. The experiment was run on a Windows system with Intel(R) Core (TM) i7-5930K CPU @ 3.50 GHz 3.50 GHz and 32 GB RAM computer.

5.1. Results and Discussion

Here, we discuss the results of the single-based classifiers and SL model used in the experimental phase by considering their learnability, predictability of BW, and each clinical feature's influence on BW.

5.1.1. BW Prediction Models

In our dataset, neonate BW is the target variable or outcome. Given the nature of the problem as a classification task, we divided BW into two distinct classes: (LBW and NBW) based on a BW threshold of 2500 g, a criterion approved by our healthcare professionals. Neonates with BW greater or equal to 2500 g belong to the NBW class (Class 0), while those with BW less than 2500 g are categorized as belonging to the LBW class (Class 1). Our study conducted two rounds of experiments for BW prediction. Initially, we evaluated the performance of the SL model using solely physiological and lifestyle features, including fetal sex, GDM, GA, and smoking.

This initial assessment excluded nutritional features. Table 5 shows the performance evaluation results achieved through tenfold cross-validation using only common physiological features. Remarkably, the proposed SL model outperformed the other single-base machine learning classifiers, achieving an accuracy of 82.27%, a precision of 0.839, a recall of 0.821, an F1 score of 0.827, and an AUC score of 0.81. In contrast, RF exhibited comparatively lower performance, with an accuracy of 70.78%, a precision of 0.719, a recall of 0.708, an F1 score of 0.691, and an AUC of 0.70.

Subsequently, we conducted a second round of evaluation for the same SL model, this time incorporating both physiological and nutritional features. The combined feature set included fetal sex, GDM, GA, smoking, plasma folate, vitamin B12, and anemia, all of which aimed at predicting the BW class. The segment below in Table 5 presents the outcomes of the evaluation process, employing tenfold cross-validation and assessing various metrics such as accuracy, precision, recall, F1 score, and AUC. Notably, the SL model demonstrated superiority, outperforming the other single-base ML classifiers. It yielded the most favorable results with an accuracy of 95.23%, a precision of 0.960, a recall of 0.957, an F1 score of 0.950, and an AUC value of 0.95. Adding nutritional factors to the SL model yields a significant improvement of 14% in the classification rate and a significant improvement of 0.15 in the AUC score. In contrast, AdaBoost exhibited the least favorable performance, achieving an accuracy of 82.89%. The insights drawn from Table 5 underscore the significance and relevance of physiological, lifestyle, and nutritional features in predicting BW. Notably, the nutritional features exhibited a stronger association with BW predictions, as evidenced by the exceptional performance of the SL model, underscoring their promise and significance in this context.

Table 5. Performance evaluation of single-based and Super Learner Model.

Attributes	Classifiers	Accuracy (%)	Precision	Recall	F1 Score	AUC
With commonly used attributes (Sex, GDM, GA, smoking)	RF	70.78	0.719	0.708	0.691	0.70
	LightGBM	74.83	0.751	0.738	0.749	0.74
	ETs	72.37	0.743	0.722	0.712	0.71
	AdaBoost	77.13	0.786	0.764	0.741	0.76
	SL	**82.27**	**0.839**	**0.821**	**0.827**	**0.81**
All clinical attributes (Sex, GDM, Vitamin B12, GA, Anemia Status, and Folate)	RF	86.07	0.879	0.861	0.859	0.85
	LightGBM	89.79	0.908	0.899	0.897	0.89
	ETs	90.15	0.911	0.928	0.898	0.90
	AdaBoost	82.89	0.835	0.829	0.809	0.81
	SL	**96.19**	**0.960**	**0.957**	**0.950**	**0.96**

The SL model yielded the best performance, and their comparison was conducted with recent state-of-the-art studies' results [21,22,31,66]. The aforementioned studies perform BW classification and estimation. These studies discussed in the related work section have mainly relied on physiological features and ultrasound characteristics to predict BW. Wasif Khan et al. [22] used multiple ML models for BW classification and found that LR performed best with 90.24%, accuracy of 90.2%, recall of 87.5%, and precision and an F1 score of 0.89. In their BW classification study, the author's critical factors were hypertension, fetal sex, GDM, and GA. Using data from the Afghanistan Health and Demographic Survey, Zahirzada et al. [66] compared the performance of five widely used ML models (ANN, KNN, NB, SVM, and RF) to identify the optimal ML algorithm. The features they used were fetal sex, maternal age, socioeconomic status, smoking, region of residence, delivery by cesarean, and high blood pressure. The author evaluated multiple ML algorithms in urban and rural populations, and RF achieved the best performance. It was evaluated using four matrices: AUC and accuracy, precision, and recall. In a study conducted in Bangladesh, Borson et al. [31] employed six classification algorithms, including K-NN, SVM, LR, NB, multilayer perceptron artificial neural network (MLP-ANN), and RF, to predict infant LBW. SVM and MLP-ANN with tenfold cross-validation achieved the best accuracy. The authors used features such as BMI, literacy rate, wealth index, number of living children, and age and split the dataset with a 75:25 ratio. The SVM obtained a precision of 0.80 and an F1 score of 0.89, while MLP-ANN achieved an accuracy of 81.67%.

Clinical and physiological characteristics are pivotal in predicting neonatal BW, as evidenced in prior research endeavors. Our experiments corroborated these findings, highlighting that model performance substantially improves with the inclusion of nutritional features. Notably, our models surpassed the performance of the above studies. This investigation reaffirmed the efficacy of the SL model, consistently demonstrating superior results. The outcomes obtained through super learners were particularly promising when nutritional features were incorporated. This signifies their potential as vital classifiers for estimating the future BW of neonates during the critical 24–27 GWs time frame, aiding healthcare practitioners and clinicians in making informed predictions. Figure 4 illustrates the performance analysis of F1 scores. As shown in Figure 4, The margin between the F1 score of the prediction of both classes is low, demonstrating accurate and balanced predictions among all classes. The SL learner achieved the best performance, and AdaBoost accessed the most minor performance among all models.

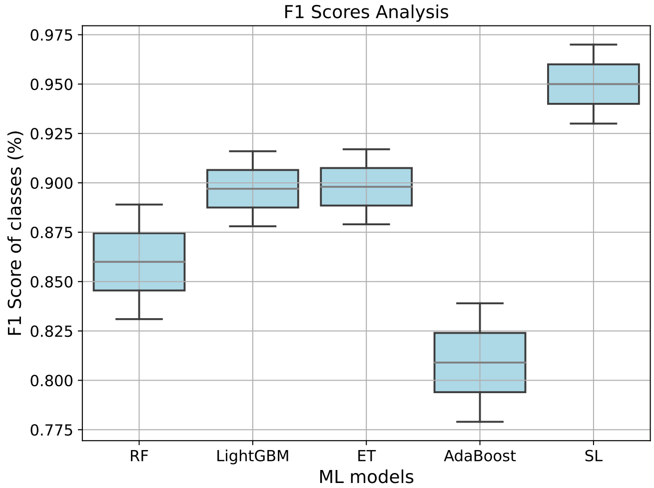

Figure 4. F1 score performance analysis of each class.

5.1.2. Comparison Between Complete and Imputed Data

Data imputation is a valuable technique employed to prevent the loss of crucial information by substituting or estimating missing values within a dataset. However, it is essential to acknowledge that imputation techniques have limitations and drawbacks. These limitations may include the potential generation of unrealistic values, data distribution alterations, and correlation between features, as highlighted by Shahjaman et al. [67]. Given these inherent limitations, researchers must carefully select data imputation techniques that effectively address these challenges.

Thus, in this section, we applied the SL model to a subset of the dataset containing 580 complete cases, which did not undergo any imputation. This allowed us to compare the results obtained using the SL model with imputed data against those achieved with complete data. This comparison served as an evaluation of the performance of our chosen imputation method, known as LI. Interestingly, the results reveal only a marginal difference between the outcomes obtained from complete and imputed data. The highest accuracy and AUC scores achieved using complete and imputed data were 89.94% and 0.89 and 96.19% and 0.96, respectively, with an improvement of 6% in accuracy and 0.07 in AUC. The comparative analysis demonstrated that LI effectively imputed the missing values while preserving realistic values and maintaining the original correlation between features. It is worth noting that the slightly higher accuracy observed in the imputed data could be attributed to the more significant number of cases in the imputed dataset, as complete data do not contain any missing values. The details of this comparison are reported in Table 6.

Table 6. Results comparison between complete and imputed data.

Dataset	Classifiers	Accuracy (%)	Precision	Recall	F1 Score	AUC
Dataset with complete cases (Without imputation)	RF	87.65	0.907	0.860	0.871	0.87
	LightGBM	83.68	0.855	0.801	0.822	0.83
	ETs	85.81	0.871	0.822	0.831	0.85
	AdaBoost	79.30	0.829	0.762	0.788	0.79
	SL	**89.94**	**0.909**	**0.882**	**0.901**	**0.89**
Dataset with imputed data	RF	86.07	0.879	0.861	0.859	0.85
	LightGBM	89.79	0.908	0.899	0.897	0.89
	ETs	90.15	0.911	0.928	0.898	0.90
	AdaBoost	82.89	0.835	0.829	0.809	0.81
	SL	**96.19**	**0.960**	**0.957**	**0.950**	**0.96**

5.1.3. Generalization of Predictive Models

In this section, we improved the generalizability of the predictive model by evaluating its performance on an independent dataset from the IEEE Child Birth Weight Cohort. Table 7 presents the results of our proposed methods on the Reus–Tarragona birth cohort, alongside a comparative analysis with the IEEE dataset, to assess the models' ability to generalize across different populations. Our proposed ensemble SL approach sustained high predictive performance, achieving an accuracy of 96.77% and an AUC score of 0.97, outperforming single-model ML approaches. Specifically, the SL model demonstrated a slight accuracy improvement of 0.58% when applied to the IEEE dataset compared with the Reus–Tarragona cohort. Both the SL and individual single-model ML approaches exhibited stability and notable enhancements in predictive performance, validating the generalization capability of our proposed method.

Table 7. Comparative Performance of the Proposed Ensemble SL Model and Single-Based ML Models on the IEEE Child Birth Weight Cohort and Reus–Tarragona Birth Cohort.

Dataset	Classifiers	Accuracy (%)	Precision	Recall	F1 Score	AUC
Reus–Tarragona Birth Cohort	RF	86.07	0.879	0.861	0.859	0.85
	LightGBM	89.79	0.908	0.899	0.897	0.89
	ETs	90.15	0.911	0.928	0.898	0.90
	AdaBoost	82.89	0.835	0.829	0.809	0.81
	SL	**96.19**	**0.960**	**0.957**	**0.950**	**0.96**
IEEE Child Birth Weight	RF	95.96	0.942	0.968	0.960	0.96
	LightGBM	93.01	0.929	0.941	0.930	0.93
	ETs	96.23	0.957	0.971	0.963	0.97
	AdaBoost	86.14	0.8578	0.8698	0.8631	0.86
	SL	**96.77**	**0.960**	**0.972**	**0.968**	**0.97**

5.1.4. Feature Importance

The term "feature importance" describes the weight given to each feature or variable in an ML model. It helps identify the most influential features in the model. The purity of the ML model's leaf nodes is a good indicator of feature importance. Figure 5c presents the importance scores of each feature as evaluated by the ETs, shown to be the most effective single-base ML model in predicting BW class with the given feature sets. The vitamin B12 feature had the most substantial influence or feature importance score among all clinical features used for BW prediction. However, plasma folate and GA had the second and third most substantial influence or feature importance scores in the evaluation by the ETs. In Figure 5a, the feature importance evaluated by RF showed that vitamin B12 had the highest feature importance score, and attributes such as folate and GA lie second and third in the feature importance ranking. The nutritional attributes, plasma folate and vitamin B12, were most influential in predicting BW by the LightGBM model. The GA attribute was the third most influential feature with smoking, fetal sex, GDM and anemia in the queue, respectively, as shown in Figure 5b. In Figure 5d, the feature importance score calculated by the AdaBoost model showed anemia and fetal sex as the least influential attributes in predicting BW and plasma vitamin B12, GA, and plasma folate as the most influential clinical attributes.

The overall assessment of feature importance computation highlighted that commonly used attributes and related features did not perform strongly in predicting BW. Specifically, features such as GA and smoking often ranked third and fourth in feature importance, while GDM and fetal sex were typically ranked fifth and sixth. Intriguingly, anemia appeared to have the lowest rank in the feature importance evaluation. Anemia in our study may be less important in the models because this is a clinically controlled feature from the first prenatal visit, treated on detection. Furthermore, from thirteen GWs until the end of pregnancy, all women are recommended to take low-dose iron supplements to prevent anemia. Given that these features are usually relied upon by physicians and featured prominently in recent research, their relatively lower importance rankings in the context of BW prediction are noteworthy. Nevertheless, it is important to note that these commonly used attributes-related features did not significantly influence BW prediction when used with the four single-base machine learning models. To illustrate, the AdaBoost model, which considered GA the second most important feature, paradoxically yielded the poorest performance among all four ML models. This discrepancy underscores the complexity of BW prediction, suggesting that additional factors, potentially including nutritional features, play a crucial role in accurate predictions.

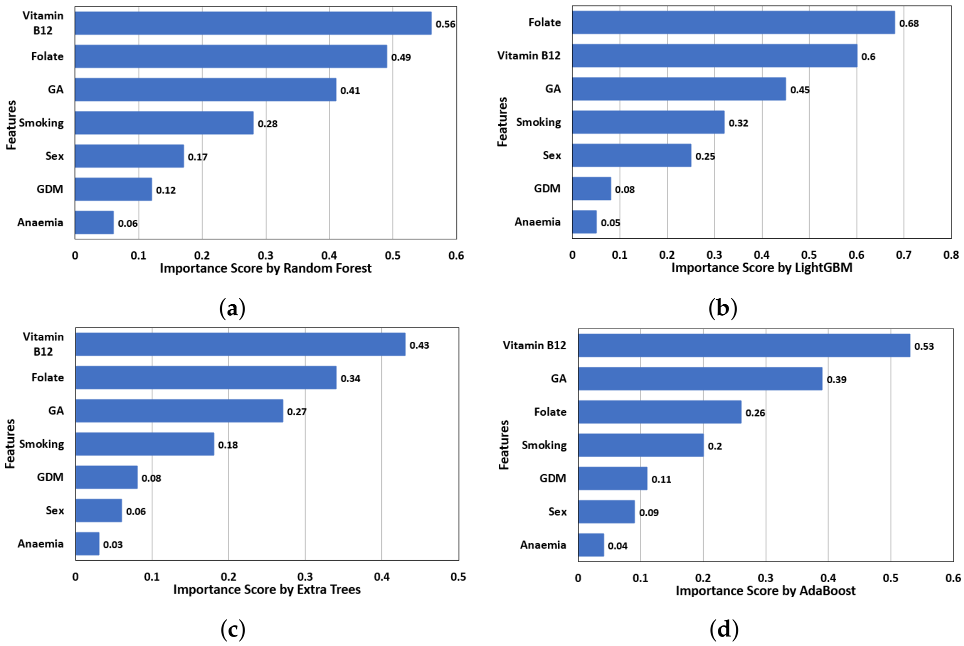

Figure 5. Feature Importance for (**a**) RF, (**b**) LightGBM, (**c**) ETs, (**d**) AdaBoost.

Regarding nutritional parameters, it was observed that maternal plasma vitamin B12 and folate status were most important when considering the RF, LightGBM, ET, and AdaBoost models. In contrast, anemia showed the lowest association among the nutritional features. When considering the amalgamation of all seven parameters, an interesting trend emerged. The model relied more on the nutritional features, enhancing predictive model performance rates than the commonly used or physiological ones. This indicates that, in this particular context, the inclusion of nutritional attributes significantly influenced the model's predictions, potentially shifting the focus away from the typically emphasized physiological factors.

The feature importance analysis illustrates the significant influence of nutritional attributes on BW prediction. As a result, we can consider incorporating a warning system into BW prediction tools to signal maternal deficiencies in vitamin B12 and folate. This alert mechanism would inform physicians of low folate and vitamin B12 status in pregnant women, prompting timely intervention. Furthermore, the insights derived from this study hold the potential for developing a decision support system to predict the likelihood of LBW in pregnant women. Such a system would enable medical professionals to proactively identify pregnant women at a heightened risk of delivering LBW neonates, facilitating early intervention and improved prenatal care strategies.

Consequently, researchers should consider nutritional factors in further studies because of their significant influence in predicting BW, as the experiments have shown.

5.1.5. Impact of Features on BW

The partial dependency plots (PDP) have been used to uncover hidden patterns and understand the significance of maternal features such as fetal sex, vitamin B12 and folate status, GA, GDM, smoking, and anemia that influence a neonate's BW. The PDP shows how the BW changes as the particular feature's value changes while holding other features constant. As shown in Figure 6a, we found a significant negative association between maternal vitamin B12 maternal vitamin B12 status and neonatal weight, as babies born to mothers with low status of vitamin B12 had NBW. This may reflect maternal–fetal vitamin B12 transfer to meet fetal requirements at the expense of maternal requirements. While lower BW with increasing maternal vitamin B12 status was observed, a sharp spike in BW when maternal vitamin B12 status was high suggested that replete maternal vitamin B12 status is also associated with NBW. The medium level of maternal vitamin B12 can cause LBW, as found in this study and Figure 6a.

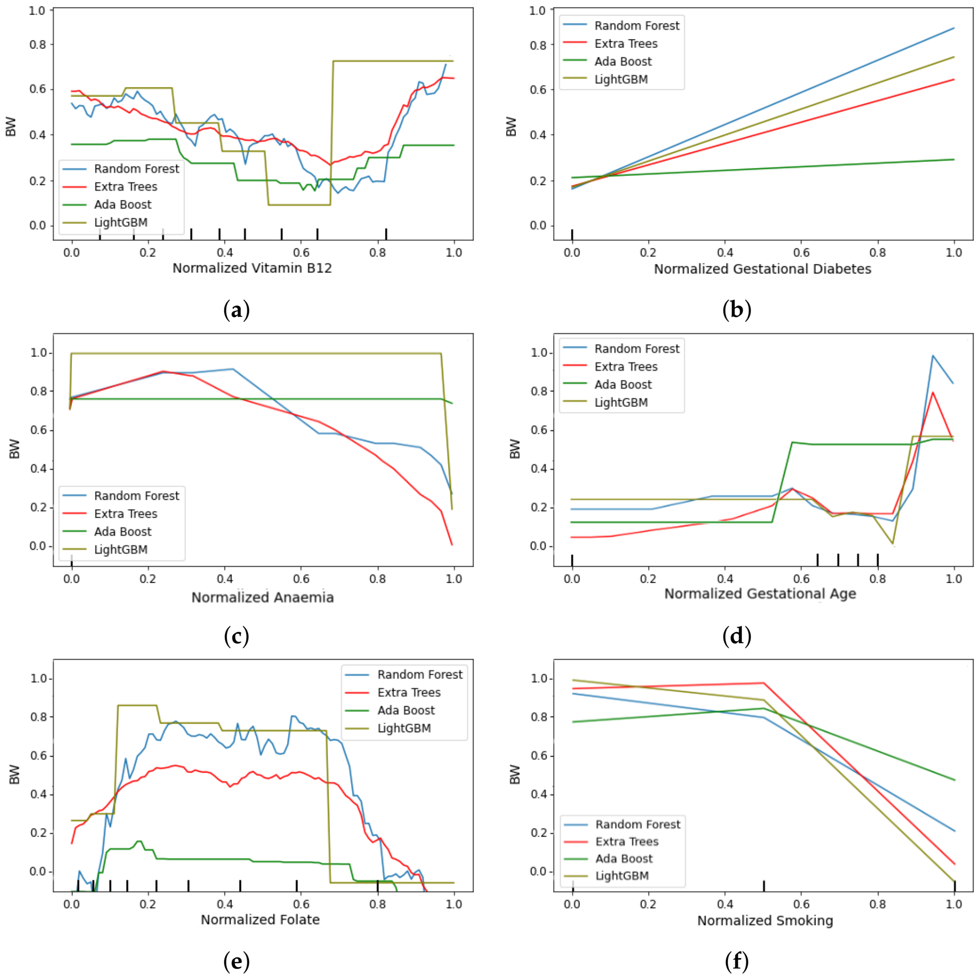

Figure 6. Panels show the impact of normalized (**a**) Vitamin B12, (**b**) Gestational Diabetes, (**c**) Anemia, (**d**) Gestational Age, (**e**) Folate, and (**f**) Smoking on BW predictions across the ML models.

GDM shows a noticeable significant positive association with BW. An improvement in the BW curve line was observed for pregnancies affected by GDM (Figure 6b), and these had a high risk of producing excessive-weight neonates. The PDP curve lines of maternal anemia status show a significant negative association with BW. LBW was observed when the mother suffers from anemia, which is associated with an increased risk of LBW in neonates, as shown in Figure 6c. GA is a reliable predictor of prenatal survival and BW. As GA progresses, the fetus grows and BW improves. The plots from ML models employed to perform this study also proved this. GA demonstrated a significant positive association with BW, and the improvement in BW appears with increasing GA, as shown in Figure 6d. Figure 6e shows the non-linear association of maternal folate with BW. Both low and high maternal folate statuses were inversely associated with BW. The moderate maternal folate status category is positively associated with BW. Not smoking was associated with NBW in the offspring, and the two best models, RF and LightGBM, show a slight decline in BW when the mother smokes during only the first trimester of pregnancy. Hence, when the mother smoked throughout the pregnancy, BW was significantly reduced (Figure 6f).

In conclusion, PDP highlighted the impact and positive–negative association of maternal characteristics such as vitamin B12, folate, anemia, GA, GDM, and smoking with neonatal BW and indicated how these maternal characteristics influence BW. This analysis could encourage doctors or clinicians to control these characteristics as part of prenatal care and for the prevention of LBW.

5.1.6. Limitations

Based on the analysis of the results, three limitations in our study should be addressed in future research:

1. Enhanced Imputation Techniques: While our study effectively utilized linear interpolation for handling missing values, future research could explore integrating advanced ML models to achieve more accurate estimations of missing data, approaching them closer to their actual values.
2. Enhanced Generalizability: Our ensemble model was trained and tested exclusively on data from two hospitals within the same geographical region. To improve the generalizability of our findings, it is imperative to conduct further assessments of the model's performance on unseen data originating from diverse areas or populations.
3. Inclusion of Additional Nutritional Factors: Further investigations should comprehensively explore various maternal indicators to gain deeper insights into the intricate relationship between maternal nutritional status and neonatal BW.

Despite these limitations, our work contributes valuable insights into the intricate connection between maternal nutritional factors and neonatal BW, providing crucial groundwork for future research.

6. Conclusions

The aim of the study was to predict BW class and explore the impact of clinical nutritional attributes, specifically maternal folate and vitamin B12, in predicting BW. We incorporated these nutritional attributes alongside commonly used features like GA, GDM, smoking, and fetal sex into our analysis. Employing the super learner model, we conducted a comprehensive evaluation, and the results highlighted the superior performance of the super learner model compared with other single-based models.

Notably, including folate, anemia, and vitamin B12 as variables significantly enhanced the accuracy of BW class prediction using machine learning models, surpassing the performance of recent studies that primarily relied on clinical physiological attributes. Given the critical importance of BW as a marker for postnatal health and survival, our findings underscore the relevance of plasma folate and vitamin B12 as valuable indicators for healthcare professionals in predicting BW. This, in turn, has the potential to contribute to reducing the incidence of postnatal illnesses and mortality.

Future research endeavors will further refine our approach by incorporating additional attributes related to environmental and nutritional factors. This continuous exploration and refinement hold promise for advancing our understanding of neonate BW prediction and improving maternal and neonatal healthcare outcomes.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/info15110714/s1, Figure S1: Feature Correlation Heatmap.

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Institutional Review Board Statement: The Reus-Tarragona Birth Cohort Study was carried out in the Sant Joan, Reus, and Joan XXIII, Tarragona University hospitals, under the approval of the Pere Virgili Health Research Institute's (IISPV) Ethics Committee and in accordance with the Declaration of Helsinki.

Informed Consent Statement: The study was described in detail to the participants and all of them provided their signed informed consent in accordance with the IISPV Ethics Committee's requirements.

Data Availability Statement: The datasets generated during and/or analyzed during the current study are not publicly available because participant consent covers data exploration in response to hypothesis testing within a defined field and with the compromise that this will be vetted by the Principal Investigators, Drs. Murphy and Cavallé-Busquets. They are willing to provide the data to interested parties on reasonable request and agreement that it will be exploited under the terms of participant consent and following further approval by the Ethics Committees if required.

Conflicts of Interest: The authors declare no conflicts of interest.

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