

Validated predictive risk analyses for Apgar scores at 5 and 10 minutes before birth as part of the smartphone application 'BrainProtect'

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Abstract

Reduced Apgar scores at 5 and 10 minutes after birth reflect signs of circulatory centralisation in newborns and are associated with poorer neurocognition in childhood and adolescence. Therefore, predictive risk analyses conducted prior to birth may enhance risk stratification and obstetrical management to improve clinical outcome and hence psychomotor development of the newborn child. To form a basis for preventive strategies, we developed a smartphone application *BrainProtect* by first calculating a weighted pregnancy risk score based on odds ratios to quantify the adverse effects of risk factors on overall predicted psychomotor development at 4 years of age. Secondly, we used a large prospective cranial ultrasound screening database (n = 5,301) and a validation cohort (n = 508,926) to relate the weighted pregnancy risk score to predicted Apgar scores at 5 and 10 minutes. The results confirmed that weighted pregnancy risk scores provide predictive capacity for expected Apgar scores at 5 and 10 minutes in newborn infants before birth which is clinically important to improve risk stratification and develop preventive strategies for a safe delivery with unimpaired vitality.

Objective

Signs of circulatory centralisation in newborns, as reflected by reduced Apgar scores at 5 and 10 minutes after birth, are associated with poorer neurocognition outcomes in childhood and later life.^{1, 2, 3} Therefore, predictive risk analyses conducted before birth may improve risk stratification and hence obstetrical management thereby enhancing clinical outcomes and optimal psychomotor development of the newborn. To form a basis for preventive strategies, we calculated a weighted pregnancy risk score based on odds ratios to quantify the adverse effects of risk factors on overall predicted psychomotor development at 4 years of age using a large prospective cranial ultrasound screening database (n = 5,301) and related the weighted pregnancy risk score to predicted Apgar scores at 5 and 10 minutes after birth as a basis to develop a predictive smartphone application.²

Study Design

A prospective cranial ultrasound screening (CUS) study was performed in a level III perinatal center on 5,301 live-born babies including 560 (10.6%) preterm infants < = 36 weeks gestation with complete records (1984–1988, predictive analysis in 2024) at discharge of the mothers.² All neonates (51.0% male) underwent CUS. In a previous account, we established that simple morphometric variables at birth and Apgar score at 10 minutes after birth predicted neurocognitive outcome at 4 years of age.² We have now examined the predictive capacity of the weighted pregnancy risk score to determine the expected Apgar score at 5 and 10 minutes before birth. Standard statistical methods, stepwise multiple regression analysis, ANOVA, ROC curve analysis and a validation procedure were employed. The study was part of a doctoral thesis (supervisor G.N.) approved by the local institutional review board of the University of Giessen and conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants, in case of minors a parent and/or legal guardian consented for study participation. This report follows the STROBE reporting guideline for observational studies.

Validation procedure

The predictive risk analyses for neonatal brain injury before birth were validated by relating the pregnancy risk score to the morphometric vitality index (MVI) at birth, combining hard growth variables with the Apgar score at 10 mins after birth ($cMVI = [zWeight + zLength + zHead\ circumference + zWeight/Length + zApgar_{10}]/5$) in the prospective cranial ultrasound screening (CUS) database (n = 5,301) and a validation cohort derived from a population based national survey (Perinatalerhebung) from various German counties (n = 508,926). The comparison revealed that the relations between these variables were similar in the two cohorts as depicted in the Figs. 1 and 2:

CUS: $cMVI = 0.297 - 0.041 * \text{pregnancy risk score}$, SE estimate 0.001, $r = 0.743$, $n = 5,246$, $P < 0.001$

National survey: $cMVI = 0.158 - 0.036 * \text{pregnancy risk score}$, SE estimate 0.000, $r = 0.479$, $n = 502,993$, $P < 0.001$

The fact that the negative slope of the regression is slightly steeper in the prospective CUS data as compared to the national survey data resides in different risk profiles in a tertiary perinatal center as compared to the general population, e.g., the preterm birth rate was 10.6% in the CUS database while that in the national survey was only 6.4%.

The correlation between calculated Morphometric vitality index (cMVI) at birth and pregnancy risk score in 5,301 newborns is depicted ($cMVI = 0.297 - 0.041 * \text{pregnancy risk score}$, SE estimate 0.001, $r = 0.743$, $n = 5,246$, $P < 0.001$).² The Morphometric vitality index at birth, combining growth variables with Apgar score at 10 mins ($cMVI = [zWeight + zLength + zHead\ circumference + zWeight/Length + zApgar_{10}]/5$), was negatively correlated to Predictive pregnancy risk score. The individual overall pregnancy risk score was generated by addition of each documented risk factor multiplied by the respective odds ratio for adverse overall predicted (p) psychomotor development ($pTotal\ psychomotor\ development\ score = (pIntelligence\ quotient + pPorteus\ maze\ test + pNeurological\ examination\ optimality\ score)/3$) at 4.3 (SD 0.8) years of age.² The rationale for using odds ratios calculated to quantify the adverse effects of pregnancy risk factors on the overall psychomotor development resides in the fact that beyond sonographically visible brain damage like hemorrhage and white matter damage, there are microstructural changes during growth restriction not visible by cranial ultrasound resulting in poor neurocognitive performance.^{1,3,4} This invisible burden of brain damage has been accounted for by the weighted score.

The correlation between calculated Morphometric vitality index (cMVI) at birth and pregnancy risk score in 508,926 newborns is depicted ($cMVI = 0.158 - 0.036 * \text{pregnancy risk score}$, SE estimate 0.000, $r = 0.479$, $n = 502,993$, $P < 0.001$).²

The Morphometric vitality index at birth, combining growth variables with Apgar score at 10 mins ($cMVI = [zWeight + zLength + zHead$

circumference+zWeight/Length +zApgar_10]/5), was negatively correlated to Predictive pregnancy risk score. The individual overall pregnancy risk score was generated by addition of each documented risk factor multiplied by the respective odds ratio for adverse overall predicted (p) psychomotor development ($p\text{Total psychomotor development score} = (p\text{Intelligence quotient} + p\text{Porteus maze test} + p\text{Neurological examination optimality score})/3$) at 4.3 (SD 0.8) years of age.² The rational for using odds ratios calculated to quantify the adverse effects of pregnancy risk factors on the overall psychomotor development resides in the fact that beyond sonographically visible brain damage like hemorrhage and white matter damage, there are microstructural changes during growth restriction not visible by cranial ultrasound resulting in poor neurocognitive performance.^{2,3} This invisible burden of brain damage has been accounted for by the weighted score.

Results

There were mean Apgar scores of 9.68 (SD 0.84, n = 5,291) and 9.86 (SD 0.50, n = 5,287) at 5 and 10 minutes, respectively, with 34 and 4 newborns presenting low Apgar scores ≤ 5 at 5 and 10 minutes after birth. The mean sum of the odds ratios multiplied by the risk factors was 7.3 (SD 16.0), range 0-85.4, n = 5,267 and 15.5 (SD 20.4), range 1.1-85.4, n = 2,479 for the entire cohort and the risk cohort.

The key result is that the weighted pregnancy risk score correlates closely with the predicted (p) Apgar score at 5 and 10 minutes after birth, respectively ($p\text{Apgar}_5 = 9.858 - 0.024 \times \text{pregnancy risk score}$, $r = 0.798$, SE estimate 0.000, n = 5,267, $P < 0.001$) (Fig. 3a). The Receiver operating characteristics (ROC) of the predicted Apgar score at 5 minutes after birth versus the pregnancy risk score revealed a sensitivity of 95.8% at a specificity of 71.0%, AUC 0.901, n = 5,301 ($P < 0.001$), a positive predictive value (PPV) of 89.7%, and a negative predictive value (NPV) of 64.5% (Fig. 3b).

The correlation between predicted Apgar score at 5 minutes and weighted pregnancy risk score in 5,301 newborns is depicted 2 ($p\text{Apgar}_5 = 9.858 - 0.024 \times \text{pregnancy risk score}$, $r = 0.798$, SE estimate 0.000, n = 5,267, $P < 0.001$).

Stepwise multiple regression analysis with documented neonatal Apgar score at 5 minutes as dependent variable was used to determine the predictors ($\text{Apgar}_5 = 4.43 + 0.142 \times \text{gestational age} - 0.426 \times \text{cardiotocogram pathologic} - 0.181 \times \text{presentation} - 0.679 \times \text{malformation} - 0.232 \times \text{growth restriction} - 0.166 \times \text{multiples} - 0.146 \times \text{EPH syndrome} - 0.103 \times \text{prolonged or arrested labor} -$

$0.087 \times \text{bleeding vaginal} + 0.066 \times \text{premature rupture of membranes}$, $r = 0.567$, n = 5,080, $P < 0.001$). The individual overall pregnancy risk score was generated by addition of each documented risk factor multiplied by the respective odds ratio for adverse overall predicted (p) psychomotor development ($p\text{Total psychomotor development score} = (p\text{Intelligence quotient} + p\text{Porteus maze test} + p\text{Neurological examination optimality score})/3$) at 4.3 (SD 0.8) years of age.² The rational for using odds ratios calculated to quantify the adverse effects of pregnancy risk factors on the overall psychomotor

development resides in the fact that reduced Apgar scores at 5 minutes after birth are associated with poor neurocognitive performance in childhood.^{1, 2, 3} This has been accounted for by the weighted score.

Using the weighted Pregnancy risk score to detect Brain damage before birth, the sensitivity and specificity yielded 95.8% and 71.0%, respectively (AUC 0.901, n = 5,301, P < 0.001), a positive predictive value(PPV) of 89.7% and a negative predictive value(NPV) of 64.5% (n = 5,301, P > 0.001). Thus, neonatal

Apgar score at 5 minutes can be predicted before birth with substantial certainty using weighted pregnancy risk scores as a solid basis for preventive strategies both to ensure unimpaired vitality of the newborn and to improve psychomotor development in childhood.⁴

Similar results were obtained for the predicted (p) Apgar score at 10 minutes after birth ($pApgar_{10} = 9.980 - 0.014 \times \text{pregnancy risk score}$, $r = 0.786$, SE estimate 0.000, n = 5,267, P < 0.001) (Fig. 4a). The Receiver operating characteristics (ROC) of the predicted Apgar score at 10 minutes versus pregnancy risk score revealed a sensitivity of 93.4% at a specificity of 62.9%, AUC 0.851, n = 5,301 (P < 0.001), a positive predictive value(PPV) of 88.2% and a negative predictive value(NPV) of 63.2% (Fig. 4b).

The correlation between predicted Apgar score at 10 minutes and weighted pregnancy risk score in 5,301 newborns is depicted ($pApgar_{10} = 9.980 - 0.014 \times \text{pregnancy risk score}$, $r = 0.786$, SE estimate 0.000, n = 5,267, P < 0.001).² Stepwise multiple regression analysis with documented neonatal Apgar score at 10 minutes as dependent variable was used to determine the predictors ($Apgar_{10} = 6.263 + 0.095 \times \text{gestational age} - 0.214 \times \text{cardiotocogram pathologic} - 0.580 \times \text{malformation} - 0.062 \times \text{presentation} - 0.077 \times \text{growth restriction} - 0.061 \times \text{stained amniotic fluid} + 0.031 \times \text{premature rupture of membranes}$, $r = 0.552$, n = 5,076, P < 0.001). The individual overall pregnancy risk score was generated by addition of each documented risk factor multiplied by the respective odds ratio for adverse overall predicted (p) psychomotor development ($p\text{Total psychomotor development score} = (p\text{Intelligence quotient} + p\text{Porteus maze test} + p\text{Neurological examination optimality score})/3$) at 4.3 (SD 0.8) years of age.² The rationale for using odds ratios calculated to quantify the adverse effects of pregnancy risk factors on the overall psychomotor development resides in the fact that reduced Apgar scores at 10 minutes after birth are associated with poor neurocognitive performance in childhood.^{1, 2} This has been accounted for by the weighted score.

Using the weighted Pregnancy risk score to detect Brain damage before birth, the sensitivity and specificity yielded 93.4% and 62.9%, respectively (AUC 0.851, n = 5,301, P < 0.001). The positive predictive value (PPV) and the negative predicted value (NPV) were 88.2% and 63.2%, respectively. Thus, neonatal Apgar score at 10 minutes can be predicted before birth with substantial certainty using weighted pregnancy risk scores as a solid basis for preventive strategies both to ensure unimpaired vitality of the newborn and to improve psychomotor development in childhood.⁴

Development of a predictive smartphone application

Data from the present study were integrated in the algorithm of a predictive smartphone application named *BrainProtect* (www.brainprotect.de) that was designed to support pregnant women, parents, and the obstetrical staff to take preventive measures by offering an early risk analysis and developmental prognosis for the child's brain utilizing validated scientific data and user-friendly modules. These preventive measures on the patient's side may include increased attention and evaluation of pregnancy risk factors resulting in adequate compliance and medication adherence as well as in the timely decision to bank the offspring's cord blood.⁸ On the doctors' and midwives' side these risk analyses may enhance preventive obstetrical management to ensure a gentle and safe delivery of the baby.

Application Design and Concept

BrainProtect is dedicated to supporting optimal child development from the prenatal period through infancy by offering continuous monitoring and data-driven guidance for parents. Its landing page highlights the main goal, i.e., (1) safeguarding healthy development of the offspring, (2) early detection of potential developmental problems, (3) prediction of the child's neurocognitive development and progress using scientific models, (4) strict security and privacy - health and contact data are encrypted, aligning with German legal standards (Fig. 5).

The developed Smartphone Application *BrainProtect* bridges a critical gap in child brain health monitoring and early pregnancy and obstetrical risk management, combining validated science with intuitive mobile user experience for care continuity and parental empowerment to take the important decision before birth to bank their offspring's cord blood and/or to plan early support measures for their child.⁸

The solution is built around the need of expectant mothers and young families to access preventative information and practical recommendations, bridging the gap between routine home monitoring and specialized medical guidance.

Landing page

The predictive *BrainProtect* application starts with a landing page in 11 languages and an AI Assistant (Ella, Chatgpt4) trained to answer all relevant questions for expectant parents (www.brainprotect.de) featuring (a) An introductory video presentation (6 mins) of an experienced female obstetrician with subtitles in 11 different languages explaining the aim, functionality and deployment of the application. (b) Explanation of the various predictive modules: General development (i.e., the average of Motor development -, Intelligence quotient (IQ) prediction -, and Labyrinth test scores (School enrolment test, Maze test) in the first 4 years of life. (c) Monitoring pregnancy risk factors, (d) Recommendations for action and preventive measures, i.e., to take the decision to bank the cord blood of the offspring or to organize early intervention measures after birth to improve educational success at school and beyond.⁸ (e) Procedures to validate the scientific data derived from full records of a prospective cranial ultrasound screening study (n = 5.301) using the full records of the comprehensive national survey data

(Perinatalerhebung, n = 508.926). (f) Presentation of the developer team. (g) Data protection and Privacy Policy.

Prognosis Modules and Application Functionality

Key Features

- General Development Prognosis: Based on user-provided pregnancy risk factors using data from the maternity passport ('Mutterpass') documented by the outpatient doctors and midwives, the app assesses the overall developmental odds up to the age of 4 years, factoring in motor and cognitive domains.
- Motor Development Module: Based on the pregnancy risk score, the statistical probability of the future motor development is extrapolated, helping parents target coordination exercises early (early intervention).
- Cognitive Development Module: Based on the pregnancy risk score, scientific models allow for extrapolating the statistical probability of the child's individual cognitive development (IQ prediction) from validated data, thus, guiding early educational interventions.
- Labyrinth Test Module (school enrollment test, maze test): Scientific models allow for extrapolating the statistical probability of potential Labyrinth test results at 4 years of age, including the prognosis for spatial reasoning and school readiness, supporting tailored enrichment activities.
- Apgar score at 5 and 10 minutes prediction before birth Module (Premium version): Allows for enhancing prospective obstetrical risk management for a gentle and safe delivery
- Brain injury prediction of the newborn before birth Module (Premium version): Allows for the parents to take the important decision to bank the cord blood of the offspring at birth as a basis for a potential stem cell treatment in the newborn period and beyond.⁸
- Pregnancy Risk Score Calculation: Uses data from the maternity passport ('Mutterpass') to generate a risk score based on the Odds ratio for a non-optimal development aiding in decision-making and potential early intervention.
- Post delivery version: Allows for using the prediction Modules (General, motor, and IQ development and labyrinth test (maze test), after delivery by keying in the actual birth data of the newborn or child until 4 years of age.
- Recommendations & Digital Assistant: Offers tailored preventative advice and digital guidance based on current test results.

Deployment Workflow

Users proceed in three steps:

1. Register and document all relevant personal and health data in the app (pregnancy risks etc.).
2. Complete guided scientific tests and questionnaires within the app.

3. Access continuous analysis and tailored recommendations for further action regarding their child's development.

Scientific Foundation and Validation

The underlying algorithm combines developmental neuroscience, perinatal risk analysis, and a large-scale cohort dataset (over 500,000 validated cases) to forecast potential negative outcomes and inform prevention strategies, developed by a leading German medical team is supported by the non-profit organisation STOP-CP bei Kindern! e.V. (www.stop-cp.org)

Illustration

The user interface employs a clear, accessible design with simple navigation and interactive progress tracking.

The screens depict:

- Risk profile input forms.
- Developmental milestone dashboards.
- Prognosis result graphics (e.g., IQ prediction graph, labyrinth test

visualization).

- Blog of experienced Board-certified female Obstetrician on pregnancy related topics
- Digital assistant chat interface for advice and next steps.
- Technical and Data Privacy Specifications
- Compatible with iPhone, iPad, Mac, and Apple Vision (iOS 13.4+/macOS 11 + required).
- Free to download, with optional in-app purchases for advanced modules.
- Health and fitness data are encrypted and only accessible to authorized users, maintaining strict confidentiality.

Discussion and Conclusion

This validated prospective study, involving 5,301 newborns with complete obstetrical records, demonstrates that weighted pregnancy risk scores have predictive value for estimating Apgar scores at 5 and 10 minutes prior to birth.² Predicting Apgar scores before delivery is clinically significant, as it enables improved risk stratification and the implementation of preventive strategies to ensure safe delivery and unimpaired neonatal vitality—both critical foundations for healthy psychomotor development and subsequent educational success in childhood and beyond.^{1, 3, 4, 5, 6, 7, 8}

The developed predictive smartphone application, *BrainProtect* (www.brainprotect.de), addresses a critical gap in monitoring early brain health and managing pregnancy and obstetrical risks. By integrating

validated scientific evidence with an intuitive mobile interface, *BrainProtect* promotes care continuity and empowers parents to make informed decisions—such as banking their child’s cord blood or planning early developmental support measures—even before birth. ⁸

Declarations

CONFLICT OF INTEREST -

The authors report no conflict of interest.

Ethics, Consent to Participate, and Consent to Publish declarations: not applicable.

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Author Contribution

A.J. wrote MS, U.J. developed application, L-M.J. designed structure of application, E.B. reviewed MS text, G.N. designed trial on PMD

Data Availability

All data are fully available upon request.

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Figures

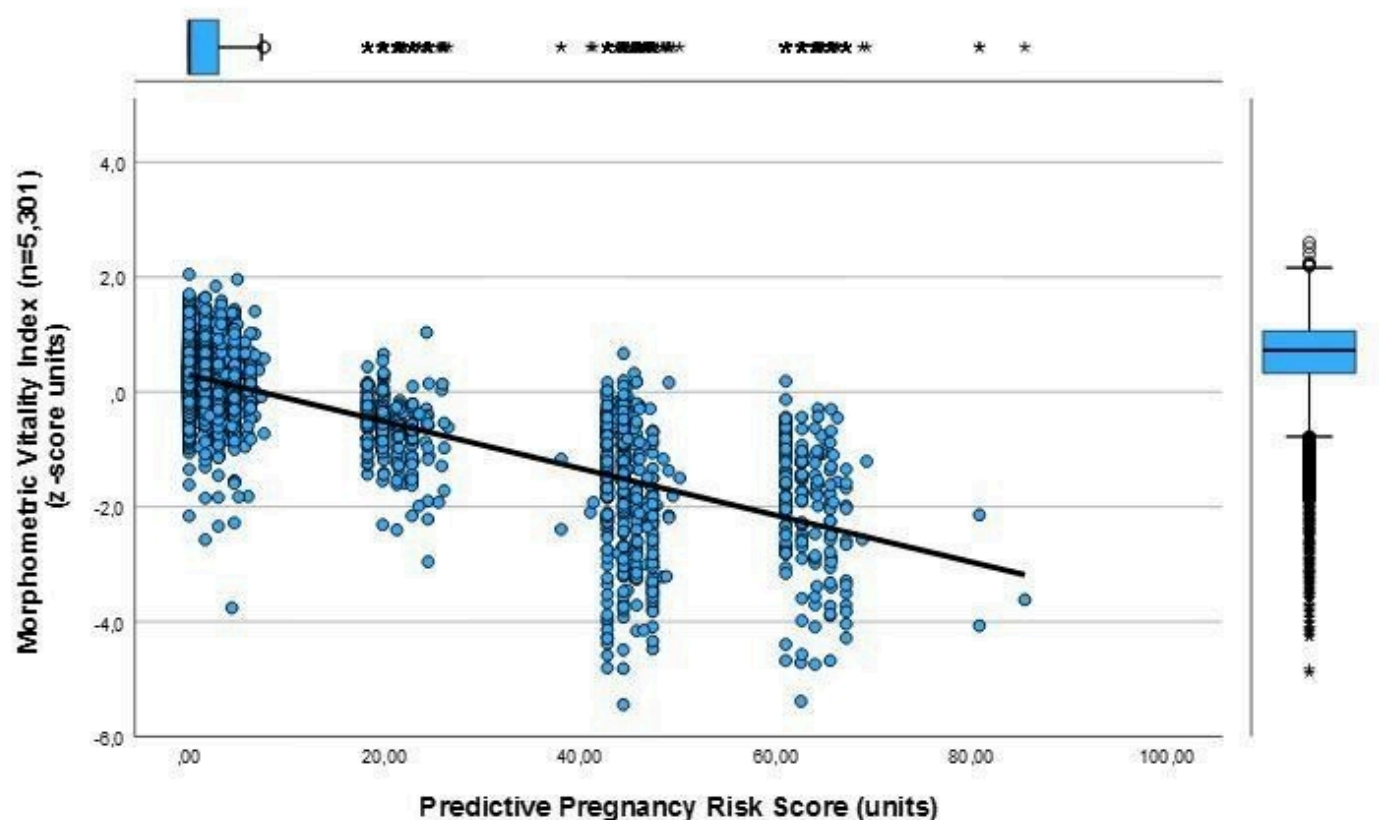


Figure 1

Relation between calculated Morphometric vitality index at birth and Predictive pregnancy risk score – Cranial ultrasound screening data (n=5,301).

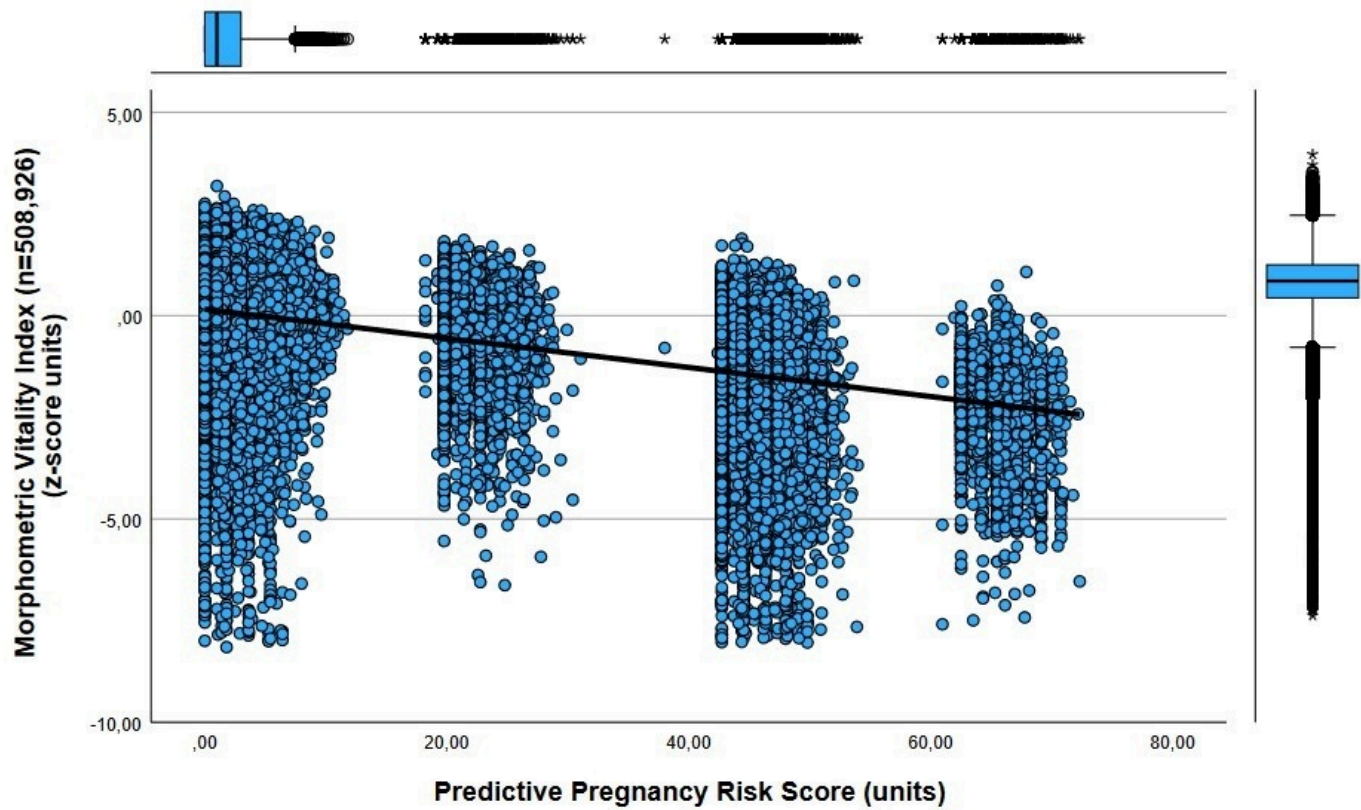
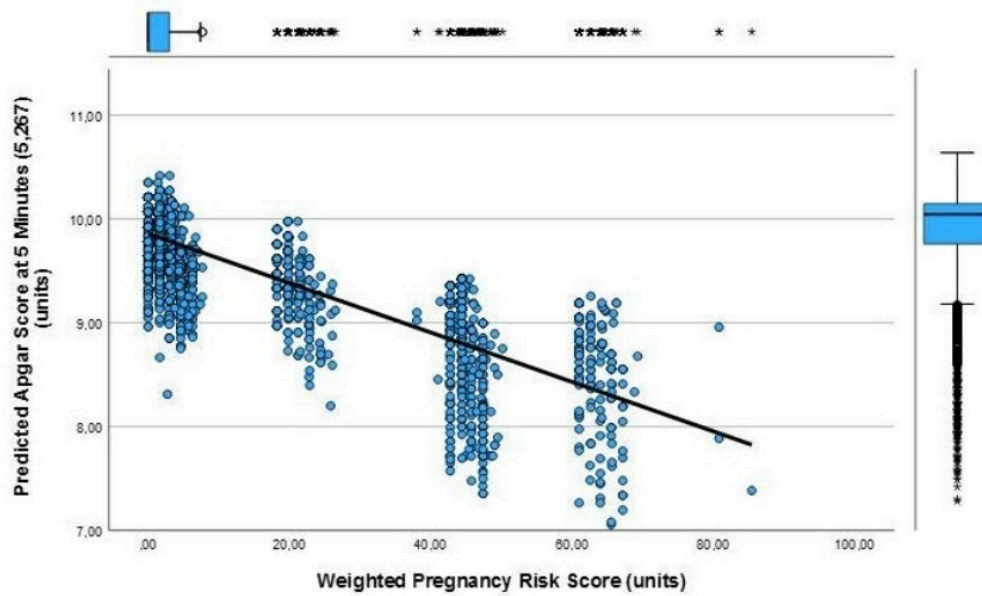
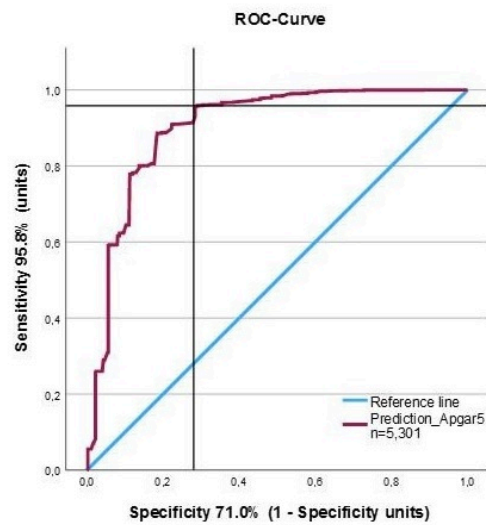


Figure 2

Relation between calculated Morphometric vitality index at birth and Predictive pregnancy risk score – Validation National survey data (n=508,926).



A



B

Figure 3

a: Relation between predicted Apgar score at 5 minutes and Pregnancy risk factors.

b: Receiver operating characteristics of predicted Apgar at 5 minutes vs. Pregnancy risk score (ROC curve analysis).

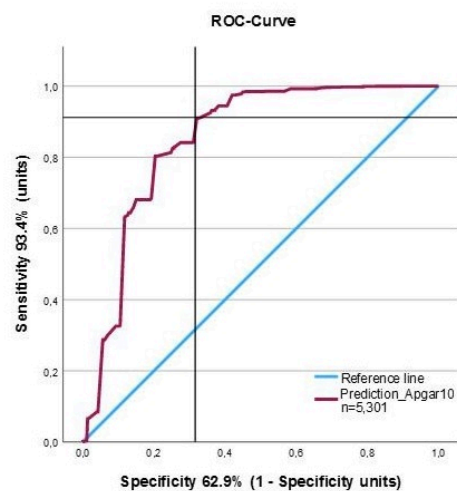
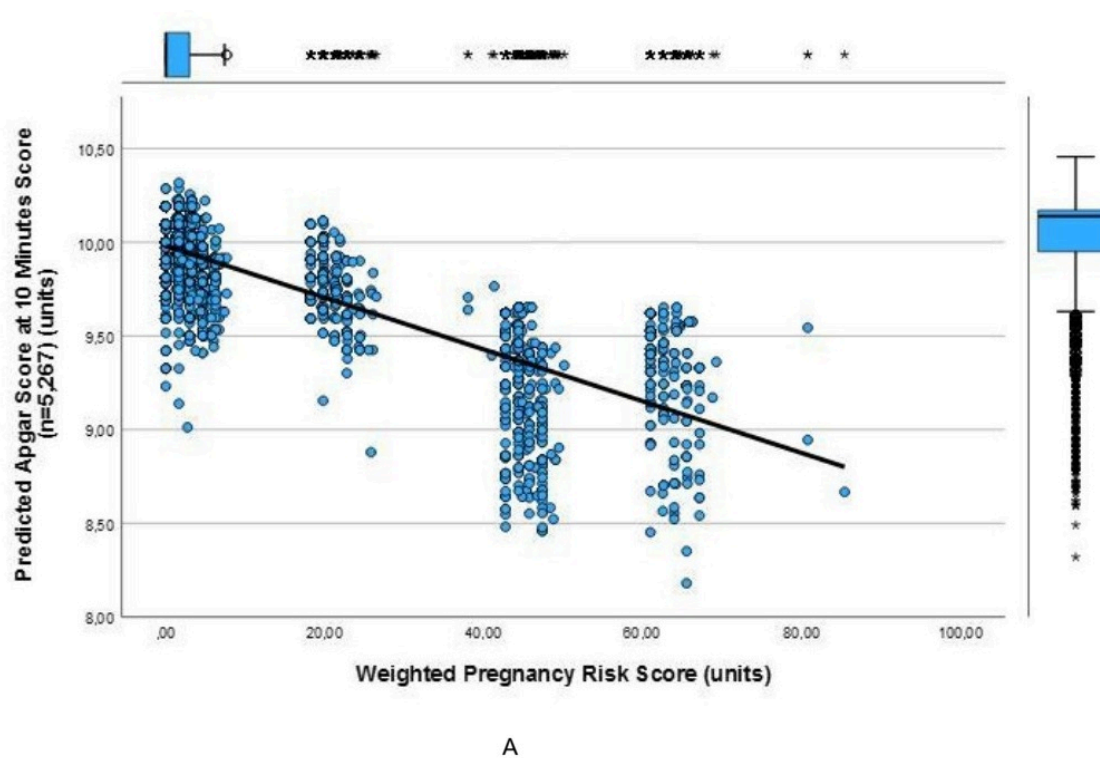


Figure 4

a: Relation between predicted Apgar score at 10 minutes and Pregnancy risk factors.

b: Receiver operating characteristics of predicted Apgar at 10 minutes vs. Pregnancy risk score (ROC curve analysis).

SCHUTZE DAS GEHIRN DEINES KINDES



Figure 5

Predictive Smartphone Application BrainProtect (www.brainprotect.de).