

Personalized Prediction of Weight Changes and Effect of Formula Milk in Neonates

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Background & Objectives

- In newborns, **physiological weight loss** during the first days of life is followed by weight gain.
- Excessive weight loss** (>8%) should be avoided as it **increases morbidity** whereas too early intervention complicates breastfeeding.
- Model published** in the Journal of Pediatrics, describing physiological weight changes¹, is **limited to healthy term neonates exclusively breastfed**.

Objectives of this work were to:

- Expand the existing model in **different neonatal populations**: late preterm and term neonates, neonates who are exclusively breastfed, exclusively formula fed or breastfed and supplemented with formula milk +/- pumped breast milk;
- Describe **effects of formula milk feeding** on neonatal weight changes during the first week of life;
- Identify and quantify **maternal and neonatal factors** influencing weight changes;
- Early forecast** individual weight changes and effects of formula milk up to 1 week of life.

Methods

- Data:**
 - Longitudinal weight data from **3638 neonates** up to 1 week of life
 - Heterogeneous population of newborns**: term, late preterm, exclusively breastfed, exclusively formula fed, breastfed with additional formula milk with or without pumped breast milk
 - Key neonatal and maternal characteristics:

Characteristics	Median [min - max] / %
Birth weight (g)	3400 [1980 - 5580]
Gestational age (GA) (weeks)	39.9 [34.4 - 42.4]
Gender: Female / Male	50% / 50%
Delivery mode: c-section / vaginal delivery	26% / 74%
Parity: 1 st child / ≥2 children	51% / 49%
Mother's age (years)	32 [15 - 51]

- Random data-splitting**: N=2425 neonates for model expansion; N=1213 neonates for advanced evaluation
- Model expansion**:
 - Expansion of the existing model by adding an effect of supplemental feeding: K-PD model, direct/indirect dose effect on additional weight gain using different mathematical functions, such as linear and Emax
 - Non-linear mixed effect modeling using Nonmem 7.3

Results

Model:

- Physiological weight change is a function of the net balance between weight gain rate **Kin(t)** and weight loss rate constant **Kout(t)**:

$$\frac{dWeight}{dt} = Kin(t) + Kin_{Add.FM} \times Dose_{FM} + Kin_{Add.PM} \times Dose_{PM} - Kout(t) \times Weight(t)$$

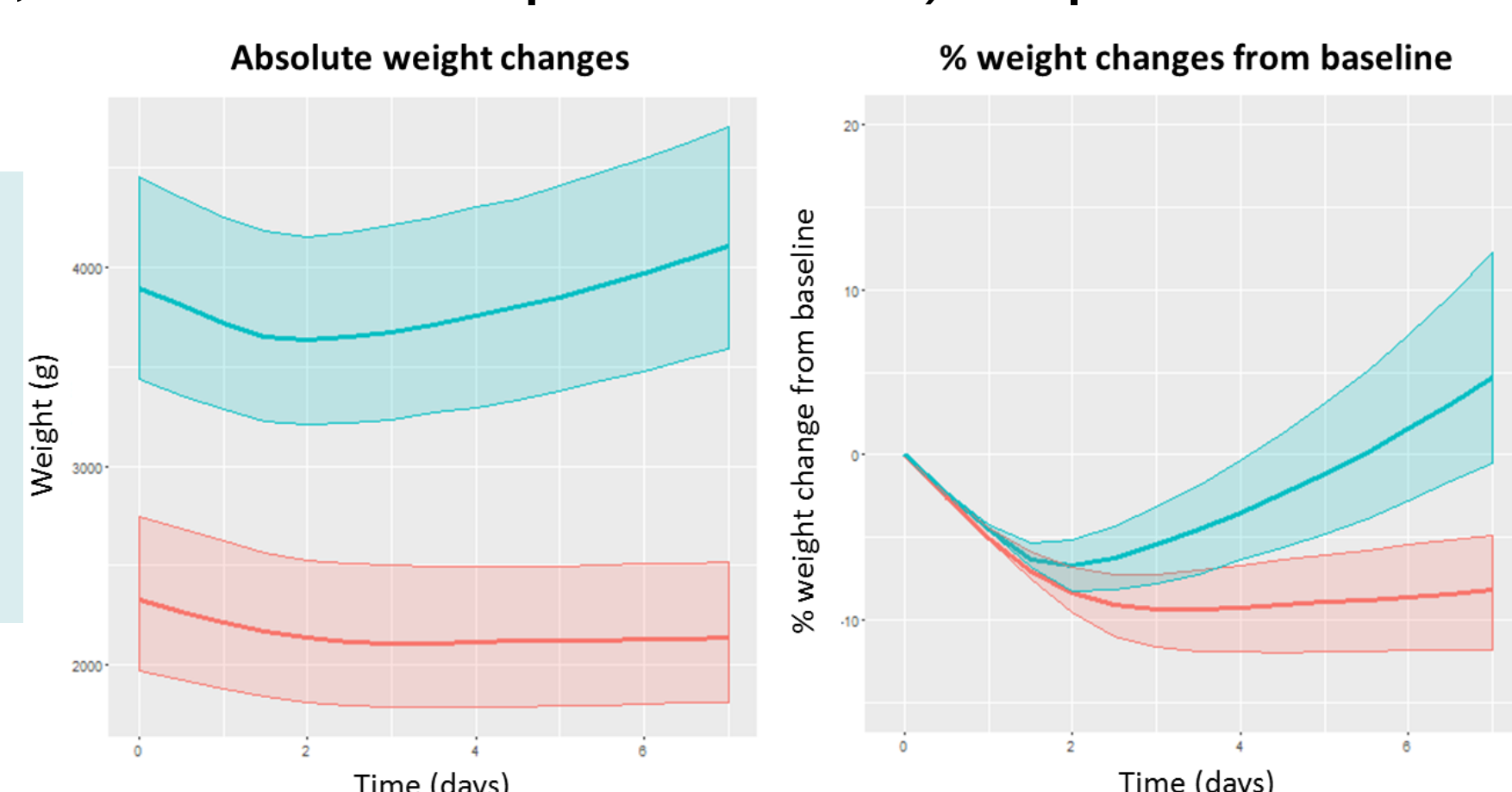
- Kin(t)**:
 - starts to increase 2 days after vaginal delivery and 3 days after cesarean section (T_{Lag})
 - 2 components: Kin_{Base} independent of time; Kin_{PNA} dependent on postnatal age (PNA)
- Kout(t)**:
 - decreases with decreasing magnitude of fluid loss
- Supplemental feeding:
 - Additional weight gain ($Kin_{Add.FM}$) dependent on dose of supplemental formula milk ($Dose_{FM}$)
 - Additional weight gain ($Kin_{Add.PM}$) dependent on dose of pumped breast milk ($Dose_{PM}$)

Covariates:

- Simulations (median, 10th and 90th percentiles) of postnatal weight changes:

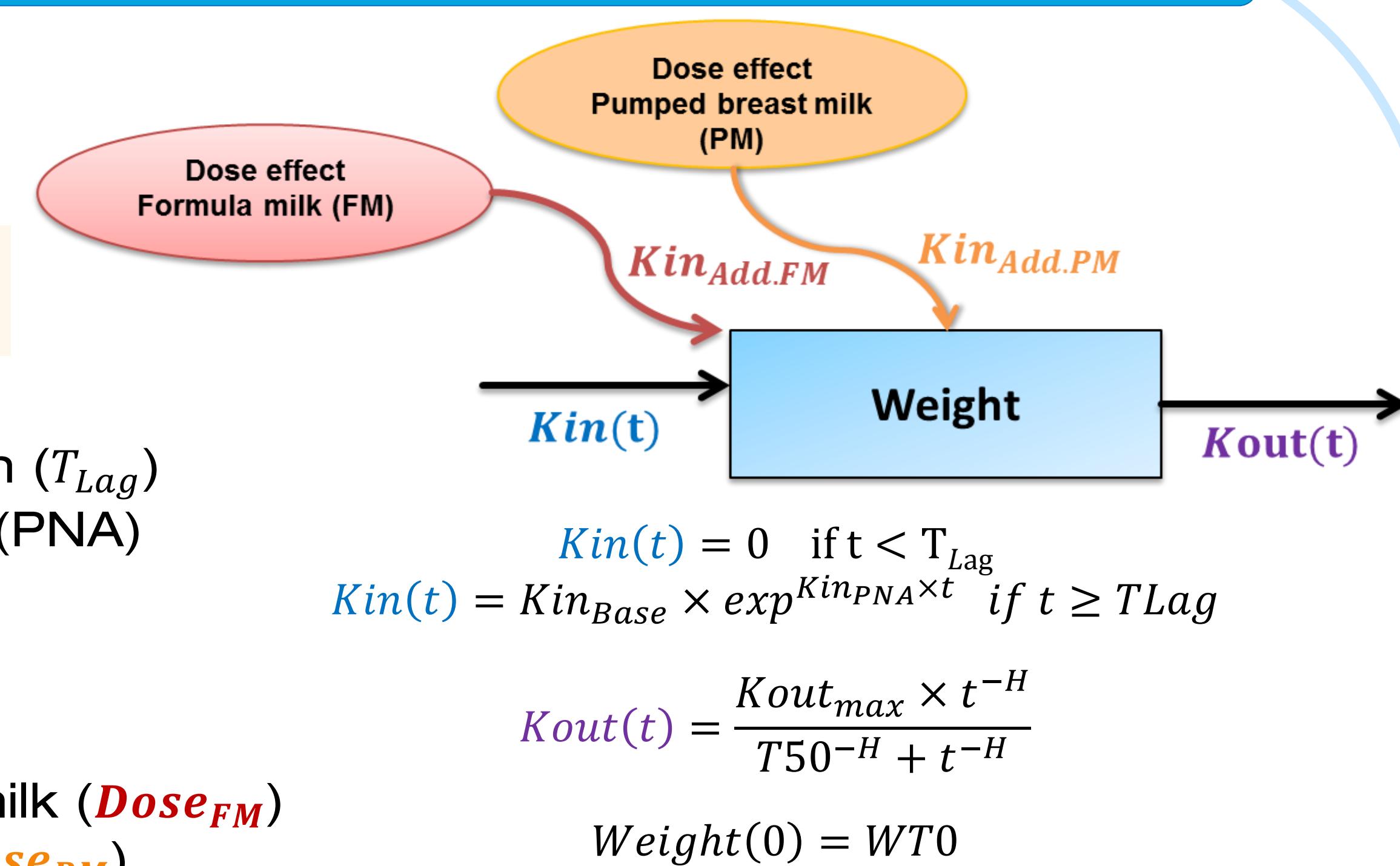
Best case scenario:

- Term: GA=42 weeks
- Male
- Exclusively breastfed
- Vaginally delivered
- Mother's age: 25 years
- Parity: 2 children



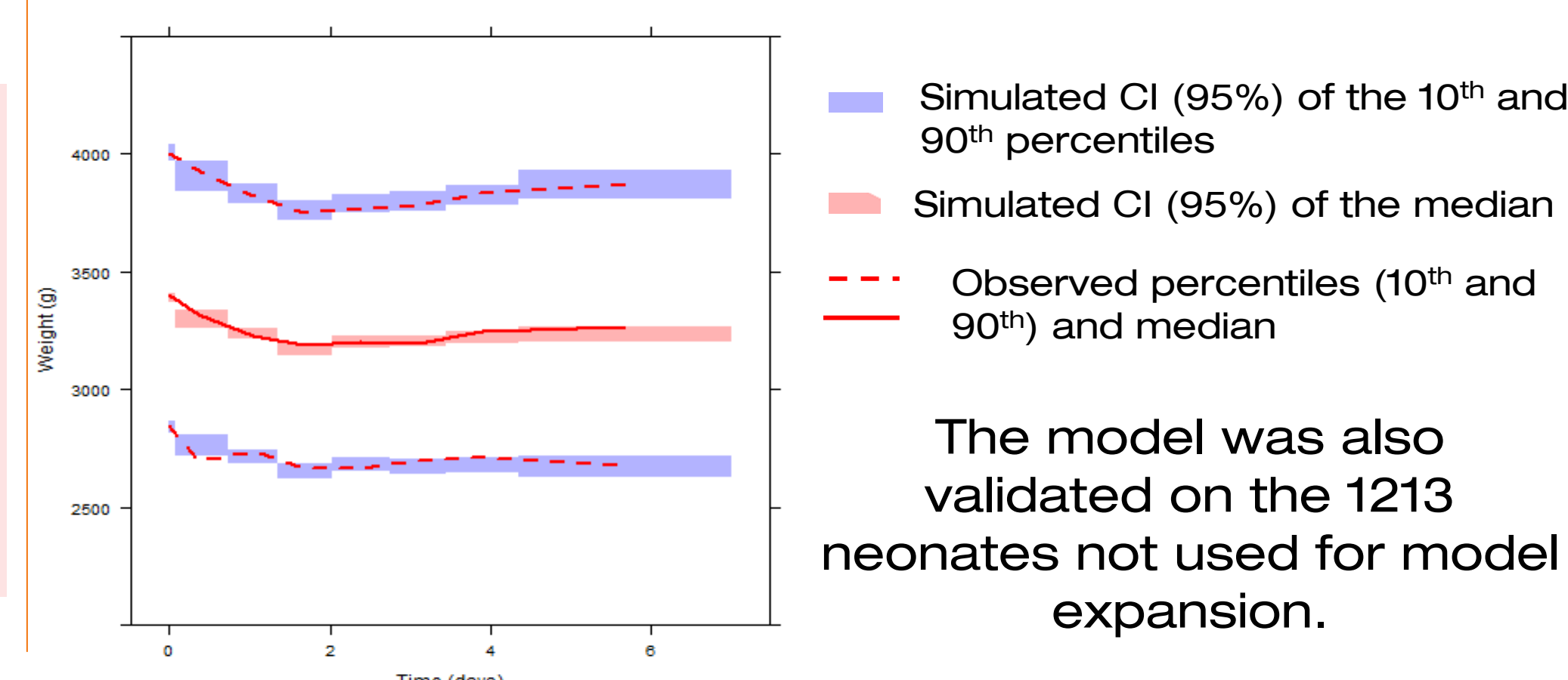
Worst case scenario:

- Pre-term: GA=34 weeks
- Female
- Breastfed with supplemental formula and pumped breast milk
- Elective cesarean section
- Mother's age: 45 years
- Parity: 1st child



Model Evaluation:

Visual Predictive Check



Clinical Application:

- Early forecast** of individual weight changes up to 1 week, based on:
 - Individual weight observations up to 3 days of life**
 - Final model**
 - Covariates**: GA, gender, delivery mode, type of feeding, mother's age, parity

Forecasted values were with acceptable **precision** and **without bias**:

MPE (Mean Percentage Error) = 0.15 %
RMSE (Root Mean Squared Error) = 61.7 g
MAPE (Mean Absolute Percentage Error) = 1.43%

Conclusion

- First model that describes **weight changes** and **effects of formula and pumped breast milk feeding** during the first week of life in **late preterm and term neonates**
- Next steps**: (i) to develop a **user-friendly online tool** to support caregivers on decision making including the use of supplemental feeding, and further personalize and optimize care of neonates; (ii) to **expand** the model in sick and very preterm neonates.