

RCSI SCHOOL of POPULATION HEALTH

An analysis of the association between maternal folic acid supplement use before pregnancy and during the first trimester and infant cognitive outcomes in a nationally representative sample from Ireland

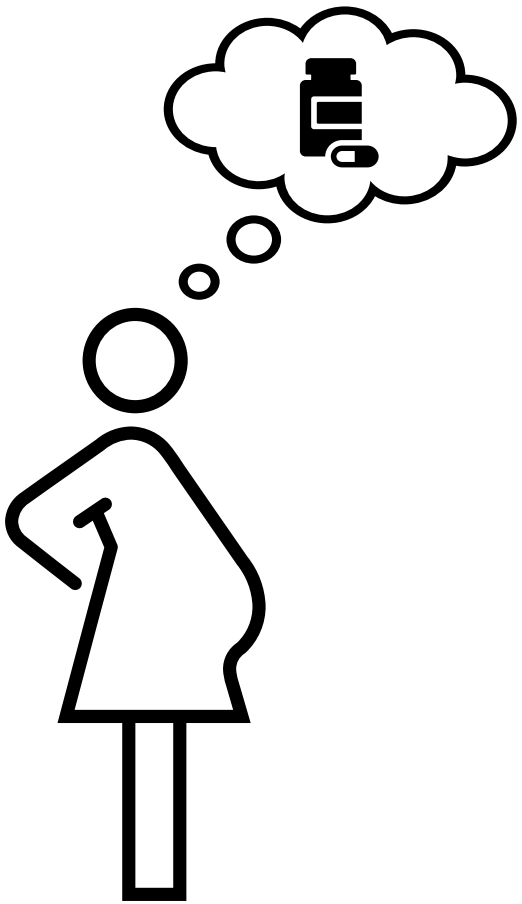
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An Phríomh-Oifig Staidrimh Central Statistics Office

Background



Folic acid supplementation before and during pregnancy **reduces the potential for neural tube defects** and other congenital abnormalities in infants (Watkins et al 1998).

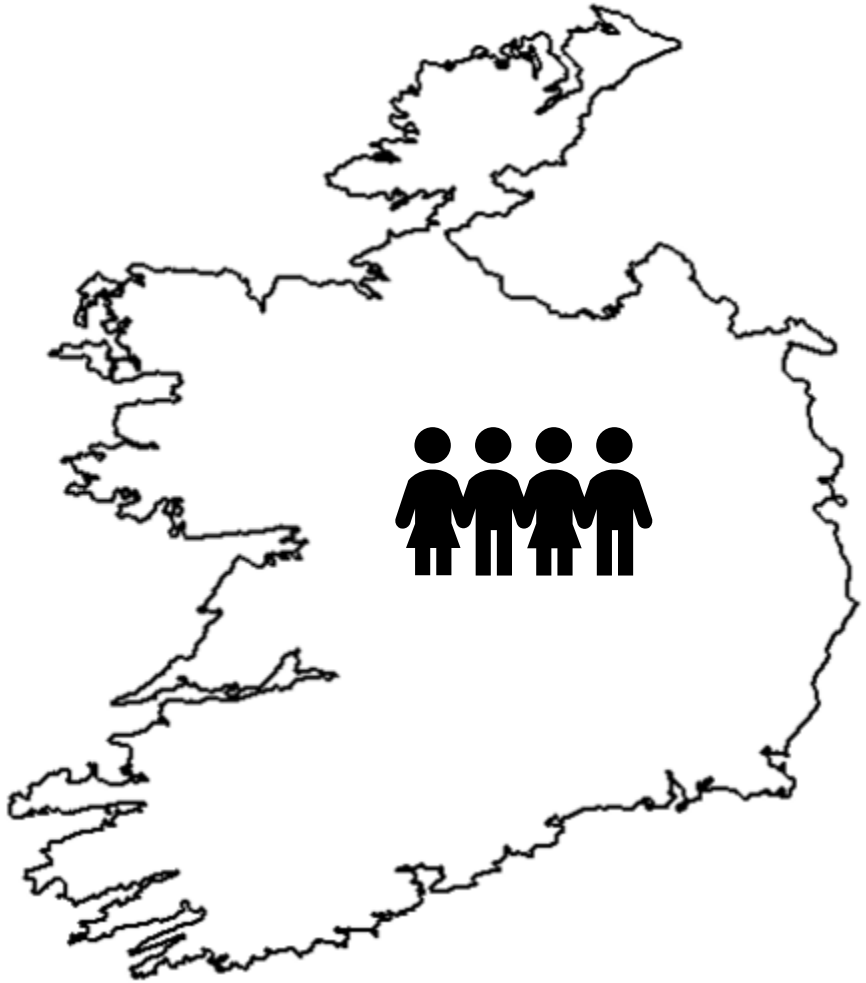
Wider neurodevelopmental benefits associated with folic acid supplementation throughout pregnancy have been reported, although **some findings are mixed**.

Current **evidence was found to be of low quality** and further research in this area was called for (Yu et al 2025)

This study therefore aimed to further our understanding of **the relationship between folic acid supplementation before pregnancy and during the first trimester and infant neurodevelopment** at 3 years and 5 years.

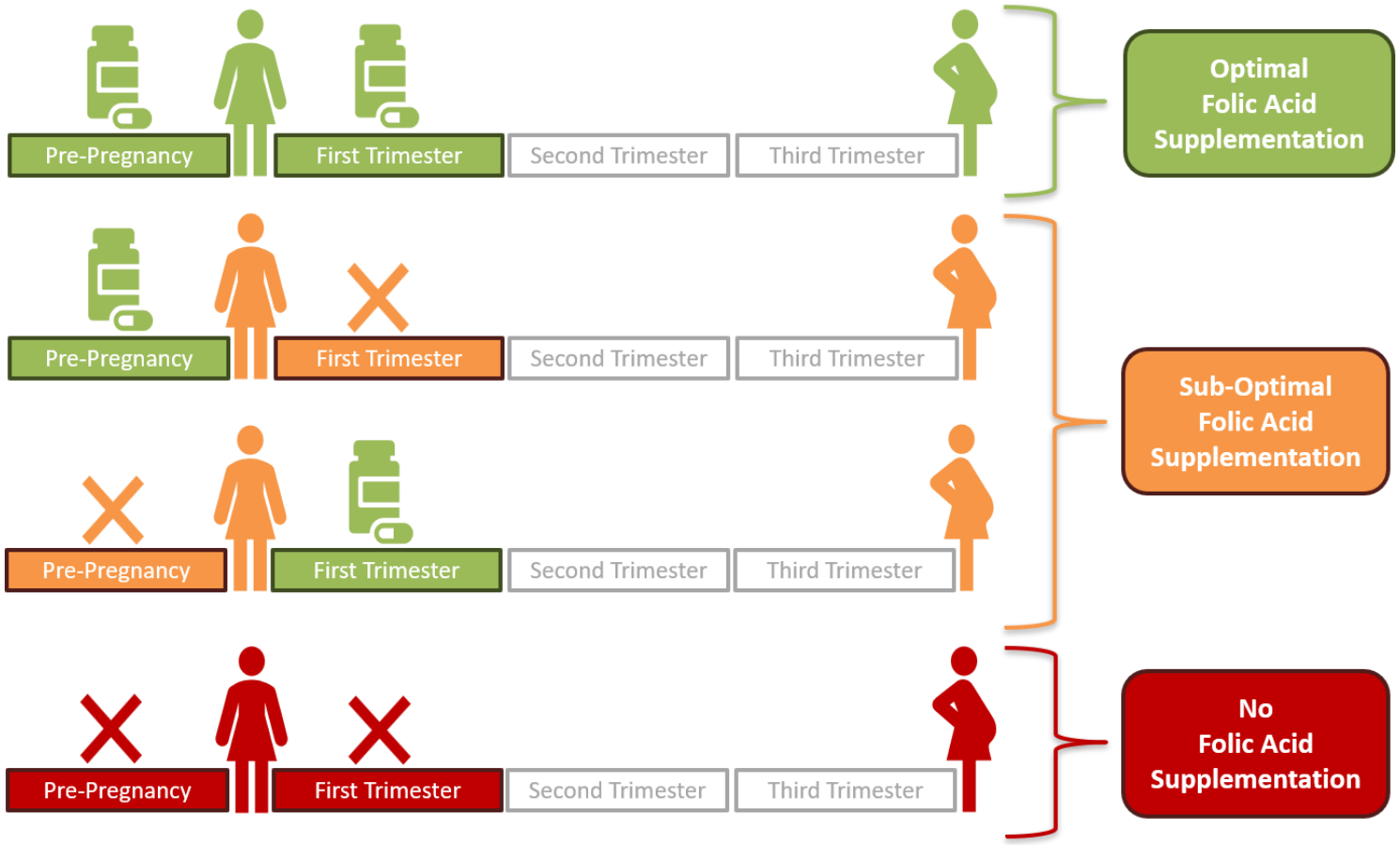
Study Population

- Data was from the **Growing Up in Ireland (GUI) study**
- First three waves of the **2008 infant cohort**
  - **Wave 1:** 9 months
  - **Wave 2:** 3 years
  - **Wave 3:** 5 years



Folic Acid Supplementation

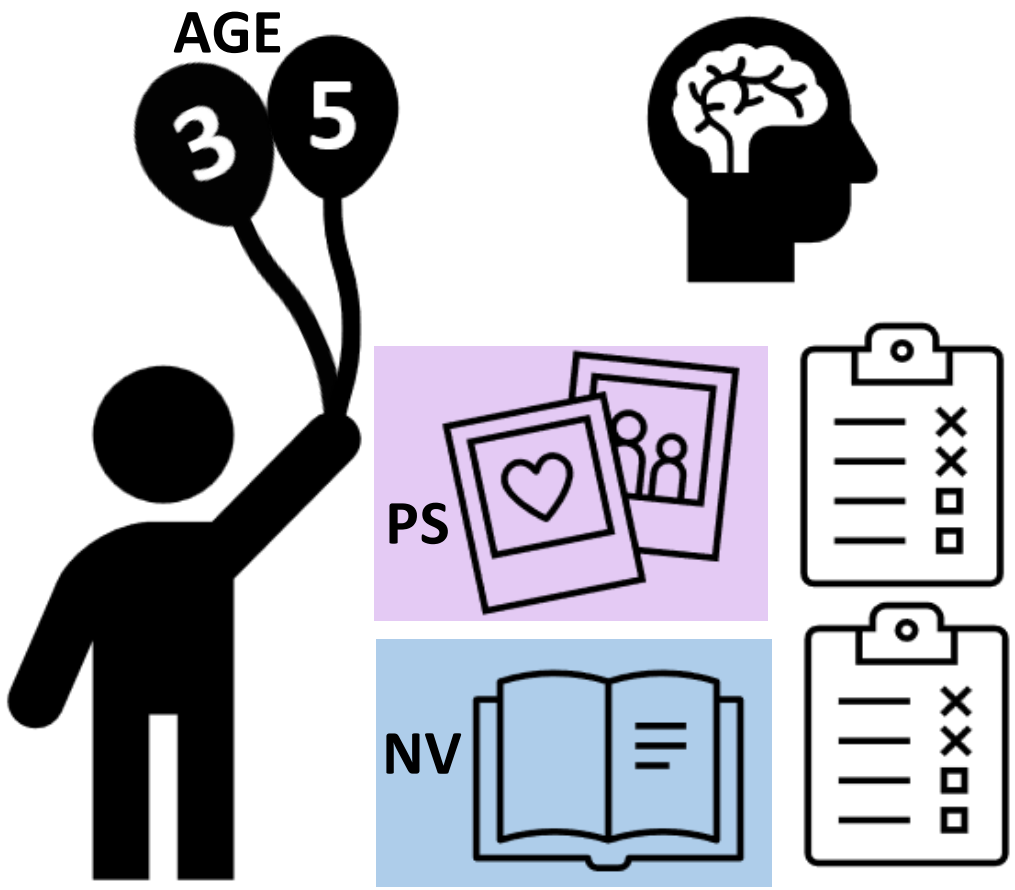
- Mothers were asked about **folic acid supplement use in pregnancy** when the infant was **9 months** (Quail et al 2011).
- We grouped folic acid supplementation **into three levels** based on the Irish guidelines for women planning pregnancy (HSE 2026)



British Ability Scale (BAS)

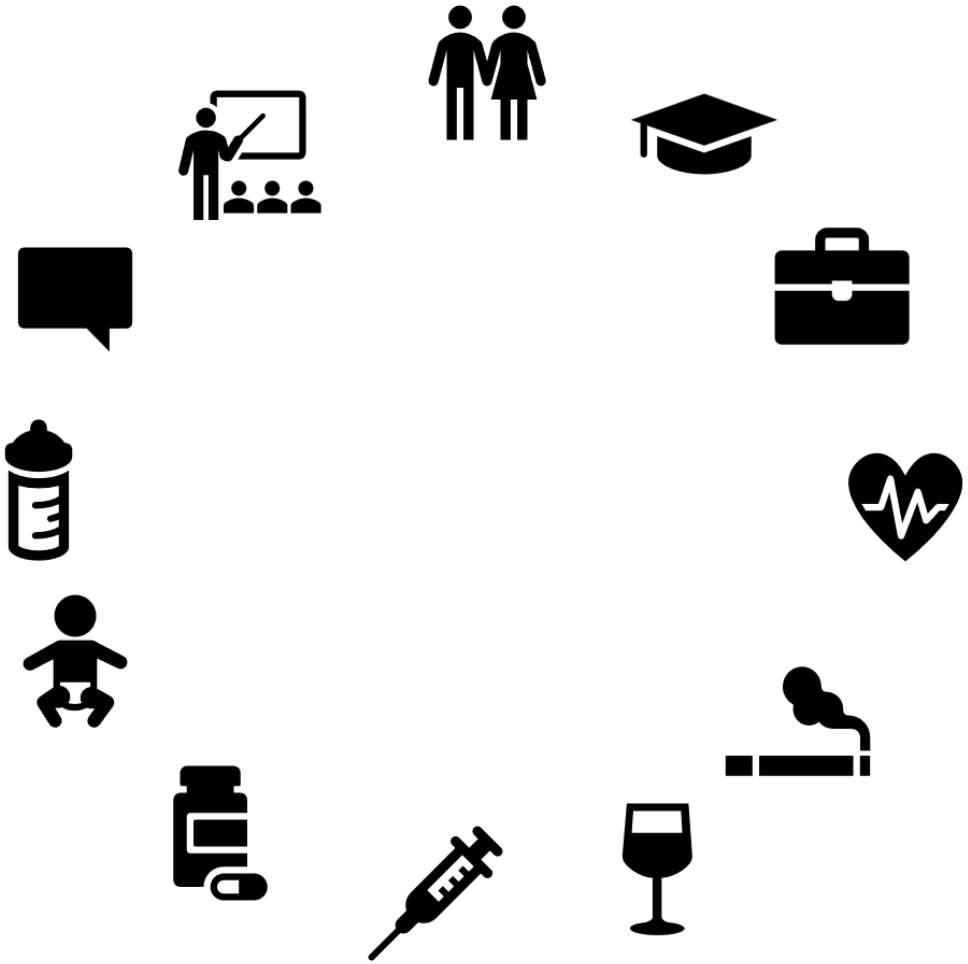
(Elliot et al 1996)

- **Picture Similarities (PS)**
- non-verbal ability
  - Four pictures were shown to the child then they were presented with a fifth card which they had a match to one of the initial four based on a shared characteristic
- **Naming Vocabulary (NV)**
- verbal ability
  - The child was asked to call out the name of an object presented to them in a picture

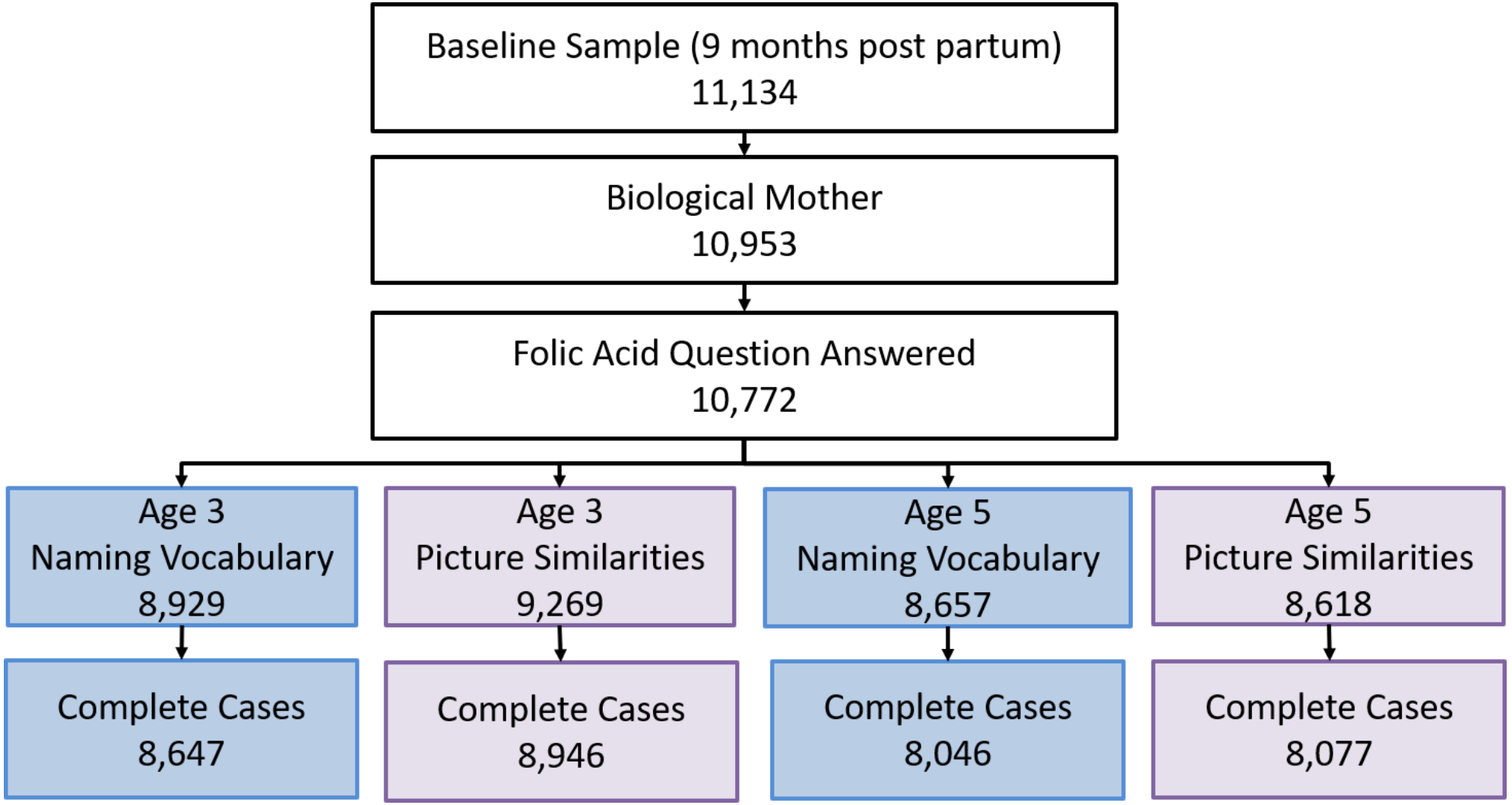


Covariates

- **Maternal Demographics**
  - Maternal Age
  - Maternal Ethnicity
  - Maternal Highest Educational Level
  - Social Class
  - Marital Status
- **Maternal Obstetric and Health History**
  - Maternal Chronic Nervous System Condition
  - Gestational Diabetes
  - Pre-Eclampsia
  - High Blood Pressure in Pregnancy
  - Parity
  - Multiplicity
- **Maternal Medication and Substance Use**
  - Iron
  - Steroids
  - Relaxants (Tranquillisers, Pills for Depression, Sleeping Pills)
  - Painkillers
  - Illicit Substances (Cannabis, Marijuana, Amphetamines, Heroin, Methadone, Crack, Cocaine)
  - Smoking
  - Alcohol
- **Infant Details**
  - Sex
  - Mode of Delivery
  - Gestational Age
  - Birthweight
  - Breastfed
  - Infant Serious Health Condition
  - First Language of Child
  - Days per week parent read to child
  - School started at age 5



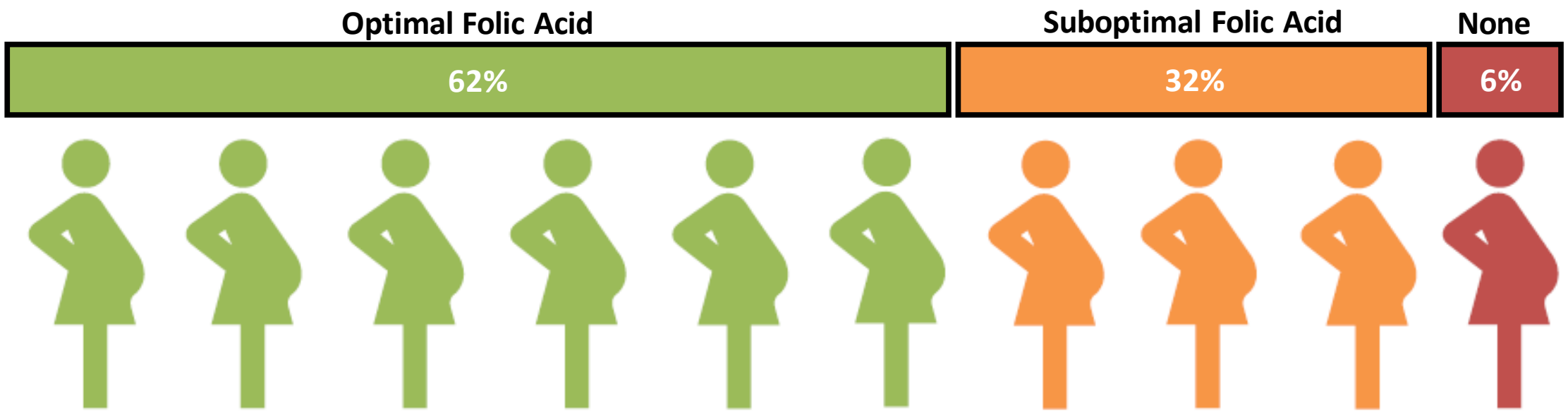
Included Sample



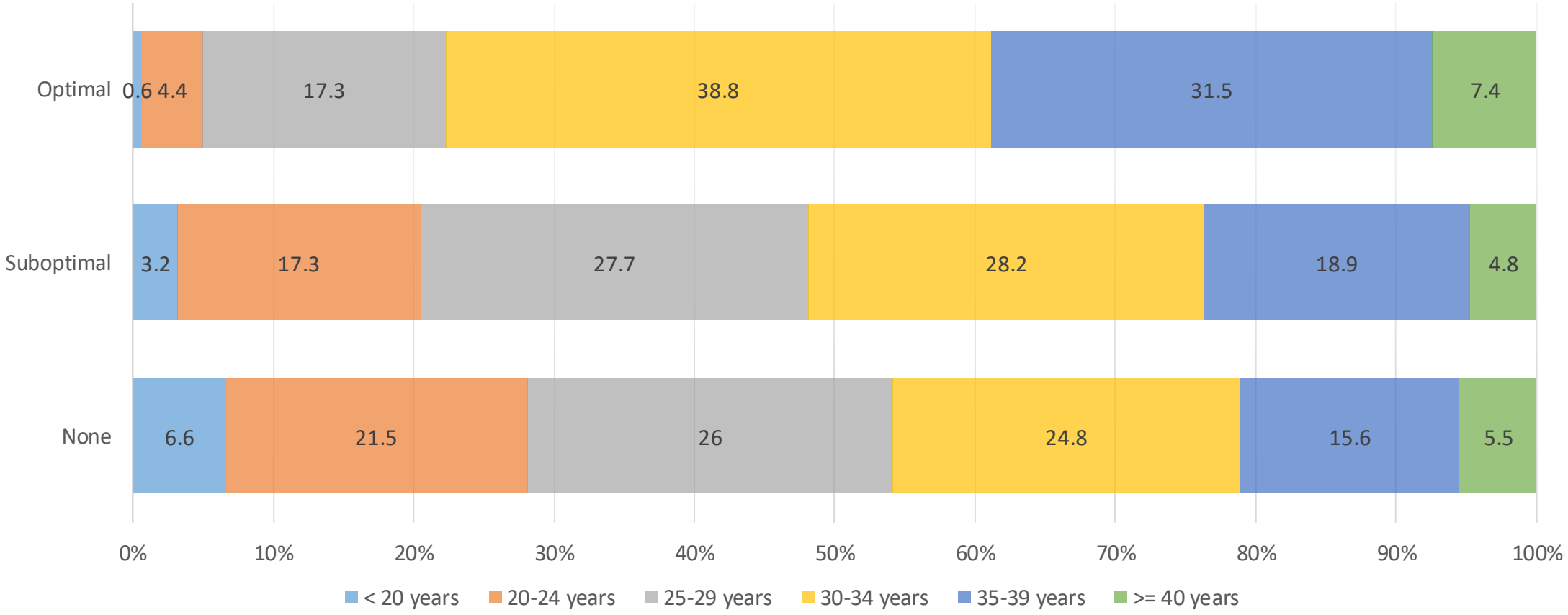
Statistical Analyses

- **Descriptive Statistics** were used to describe **the population by folic acid** supplementation group
- **Hierarchical multivariable linear regression** models were used to understand **the relationship between maternal folic acid supplementation and child score** on the BAS subscales at age 3 and age 5
  - **Model 1:** Adjusted only for **infant sex**
  - **Model 2:** Adjusted also for **maternal demographics**
  - **Model 3:** Adjusted also for **maternal health & obstetric history**
  - **Model 4:** Adjusted also for **maternal medication & substance use**
  - **Model 5:** Adjusted also for **infant characteristics**

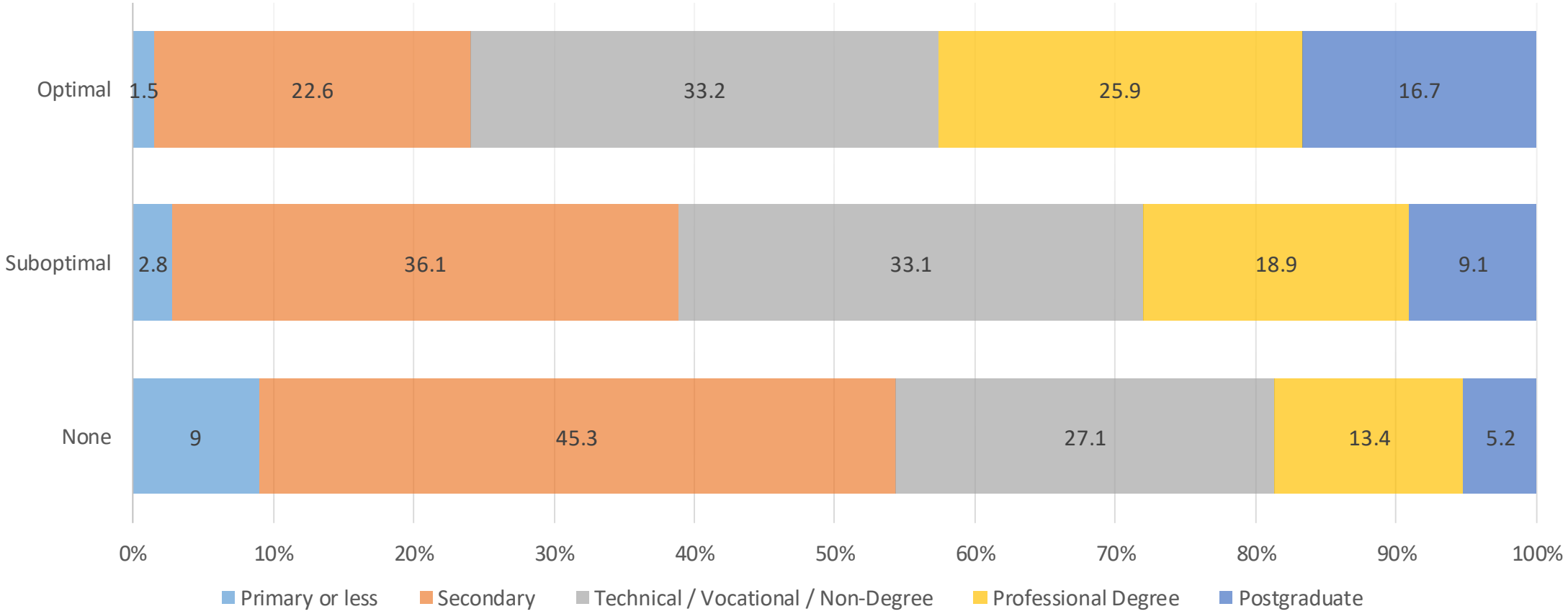
Prevalence of Folic Acid Supplementation



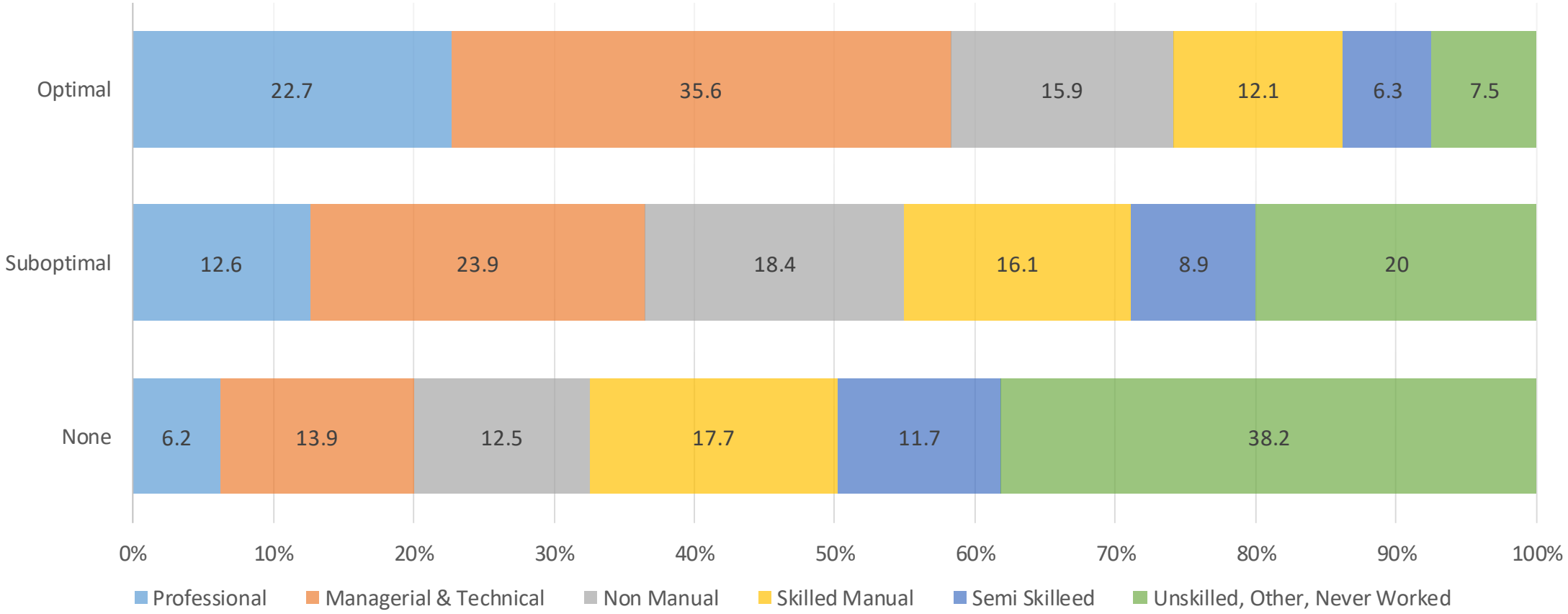
Maternal Age by Folic Acid Group



Maternal Education by Folic Acid Group

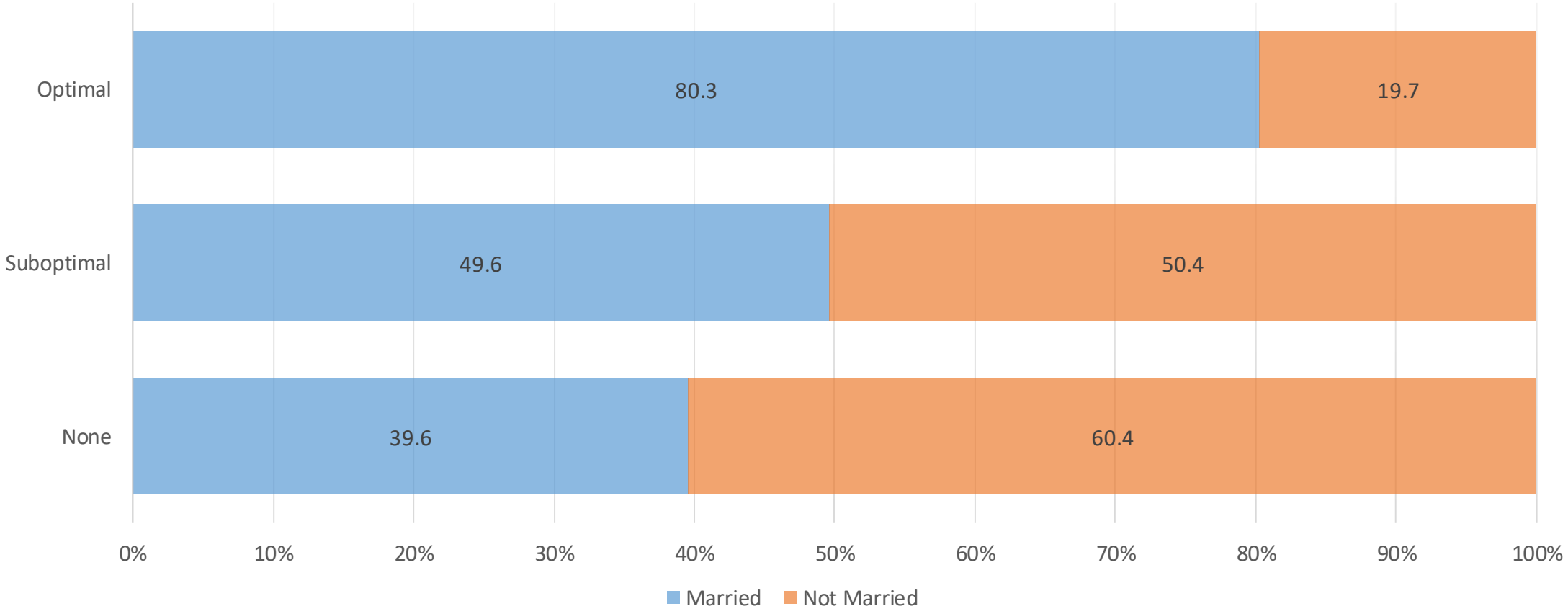


Maternal Social Class by Folic Acid Group

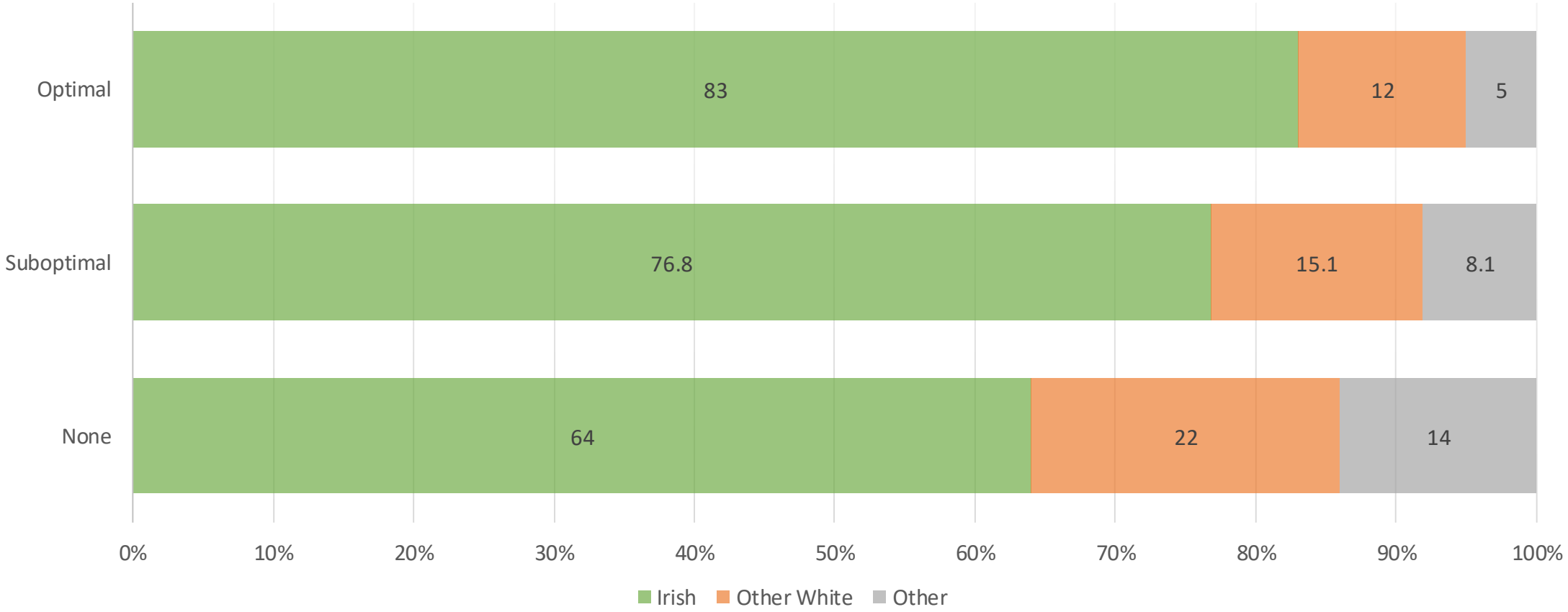


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Marital Status by Folic Acid Group

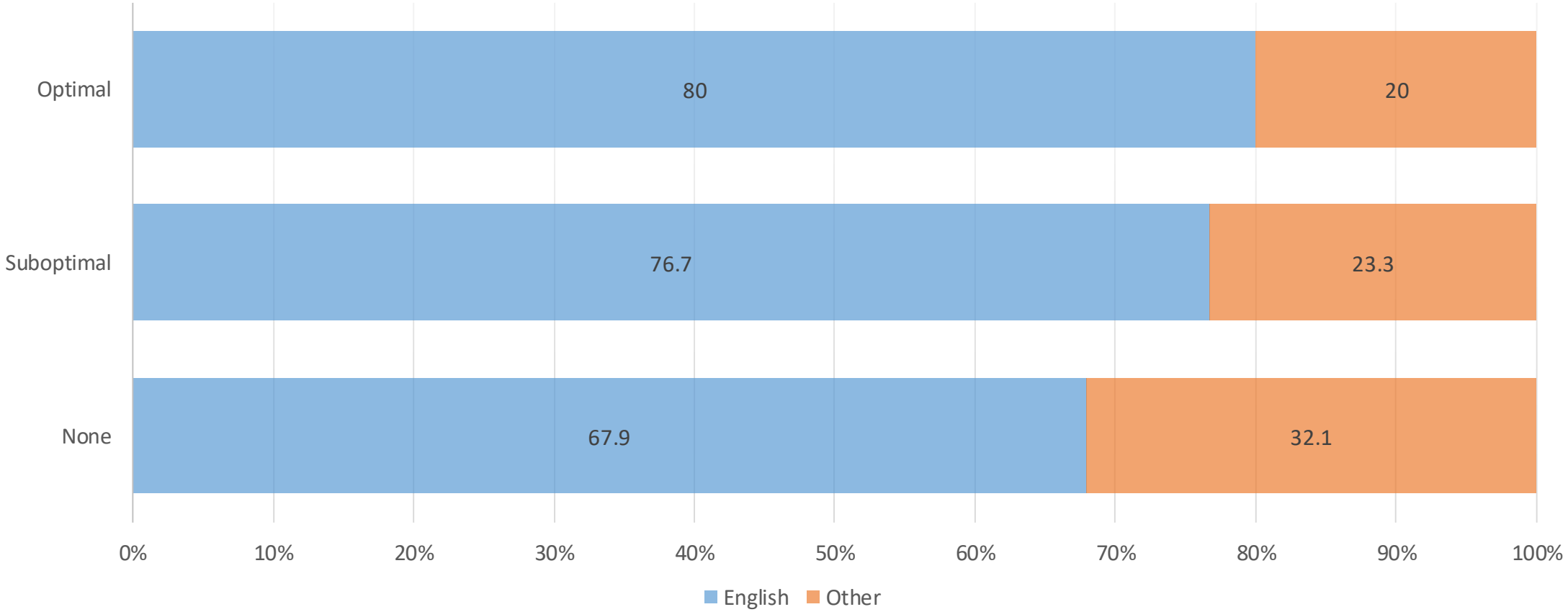


Maternal Ethnicity by Folic Acid Group



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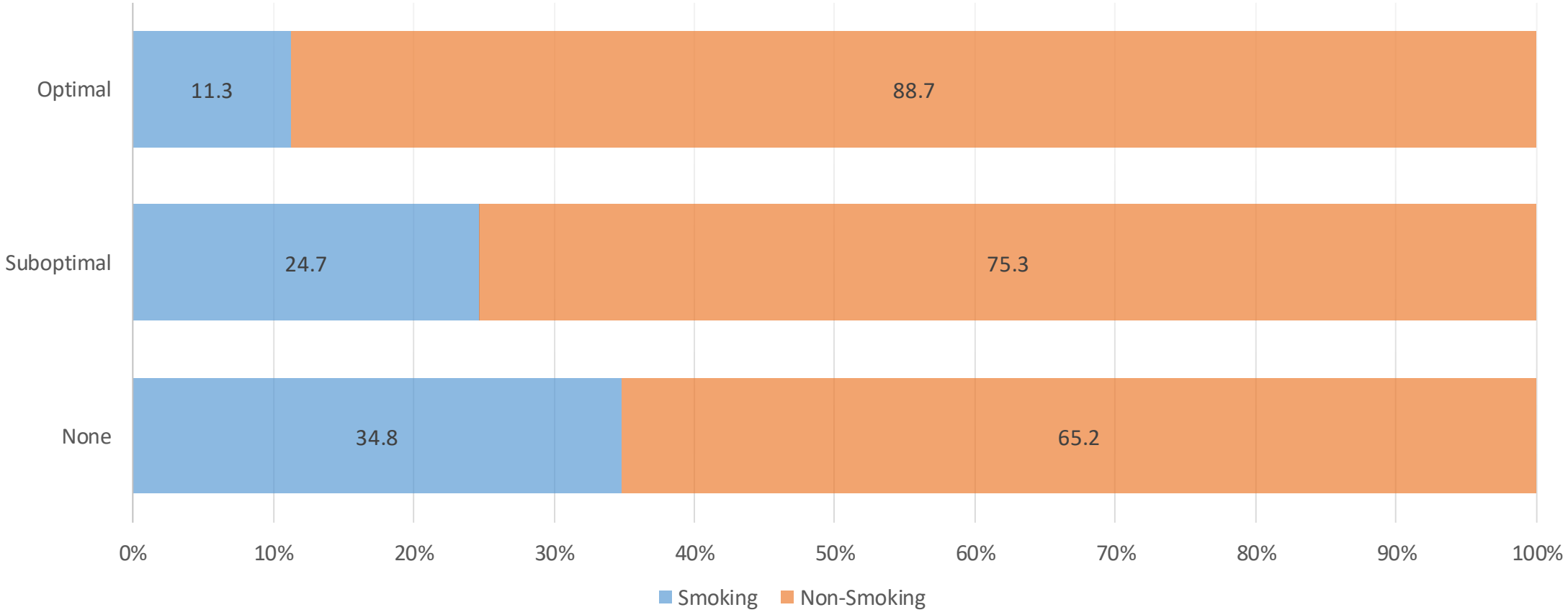
Child First Language by Folic Acid Group



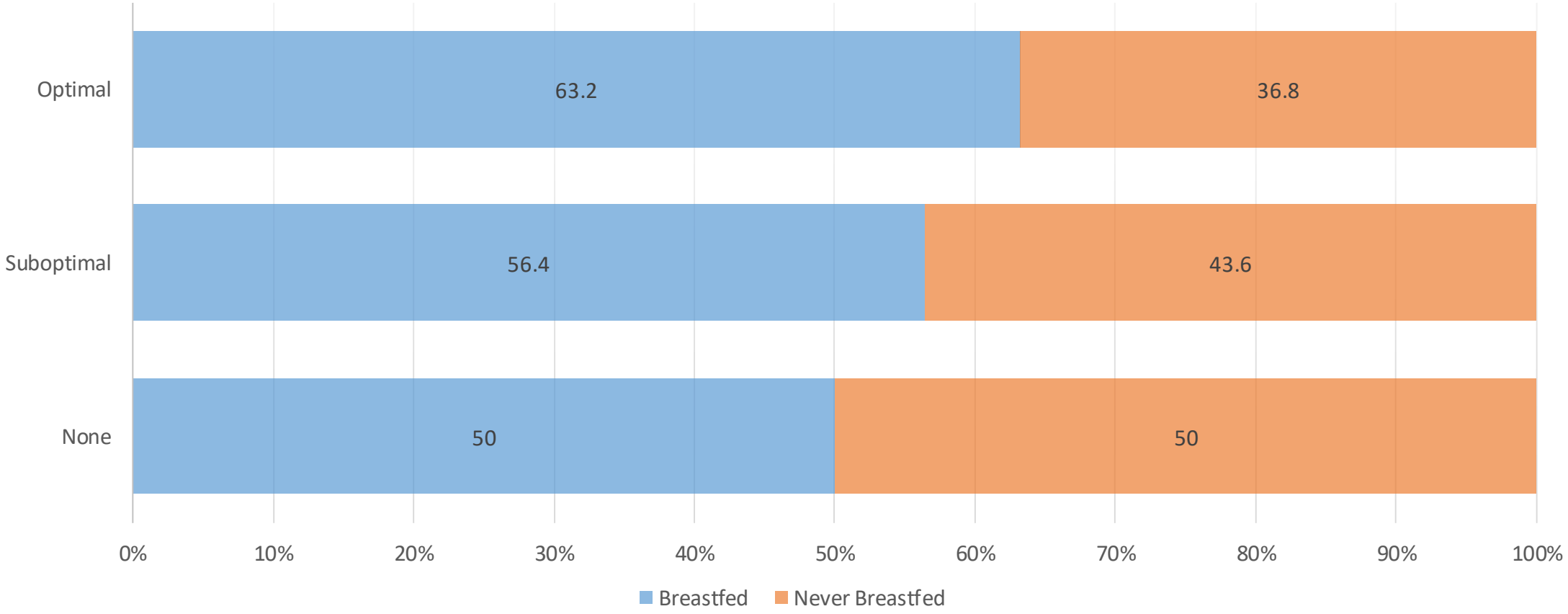
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Smoking by Folic Acid Group



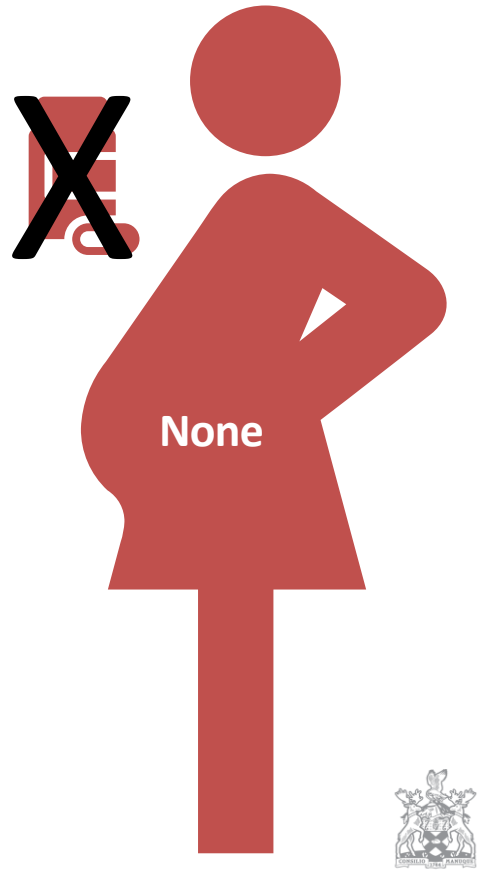
Ever Breastfed by Folic Acid Group



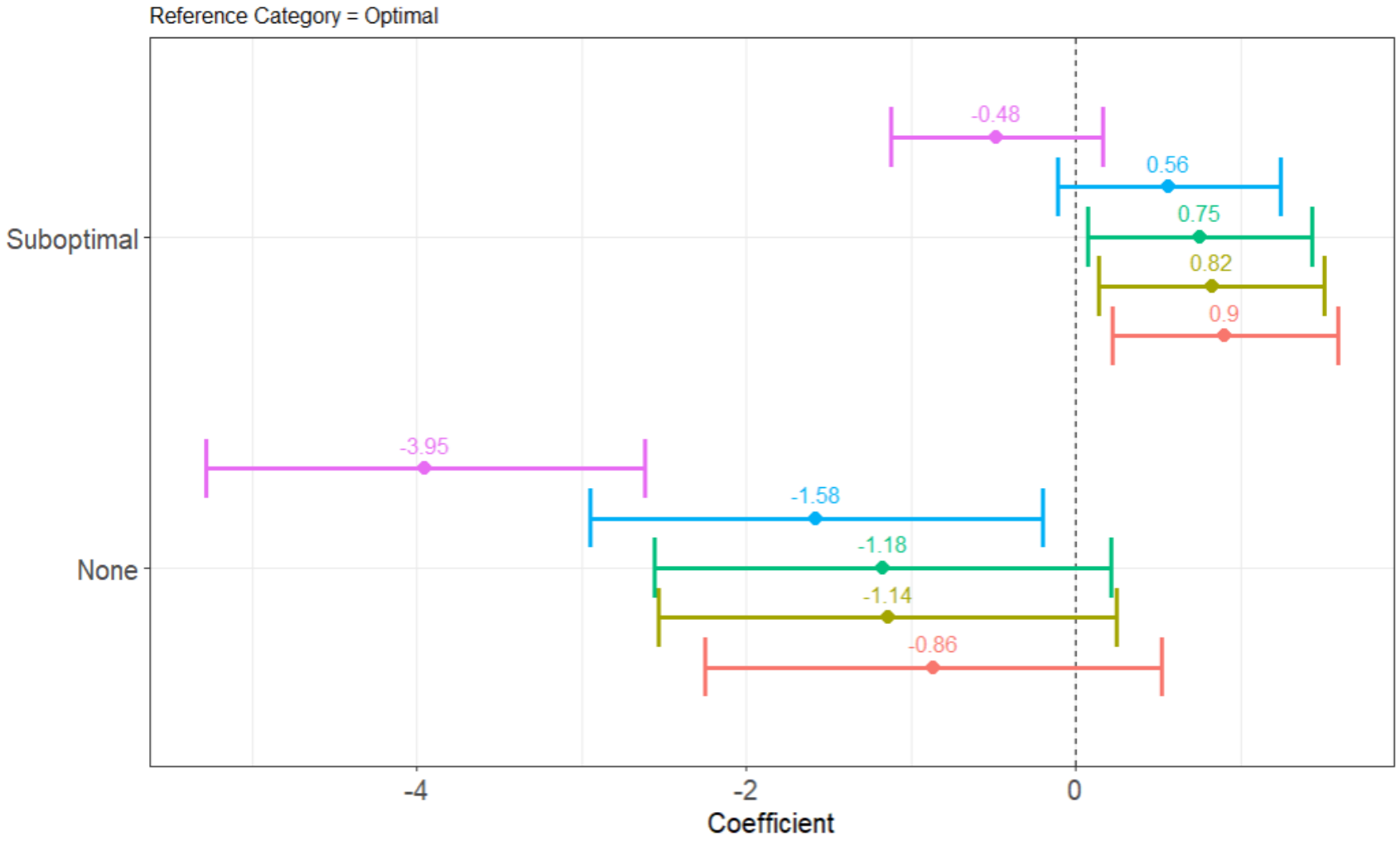
Profile by Folic Acid Group



Older	Maternal Age	Younger
Higher	Maternal Education	Lower
Higher	Social Class	Lower
Higher Proportion	Married	Lower Proportion
More Irish	Ethnicity	Less Irish
More English	Child First Language	More Non-English
Lower Proportion	Smoking in Pregnancy	Higher Proportion
Higher Proportion	Breastfed	Lower Proportion

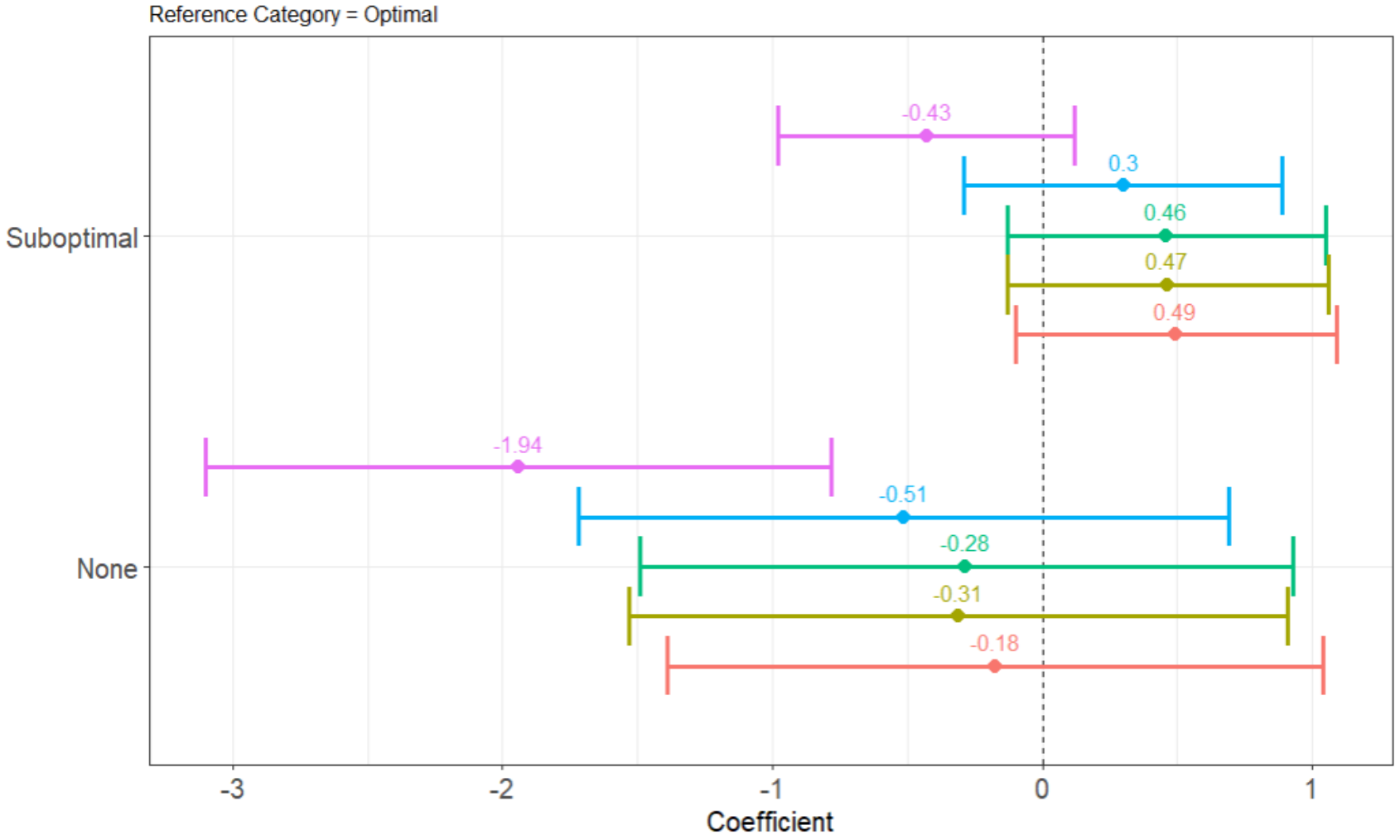


Picture Similarities Age 3 (n=8946)



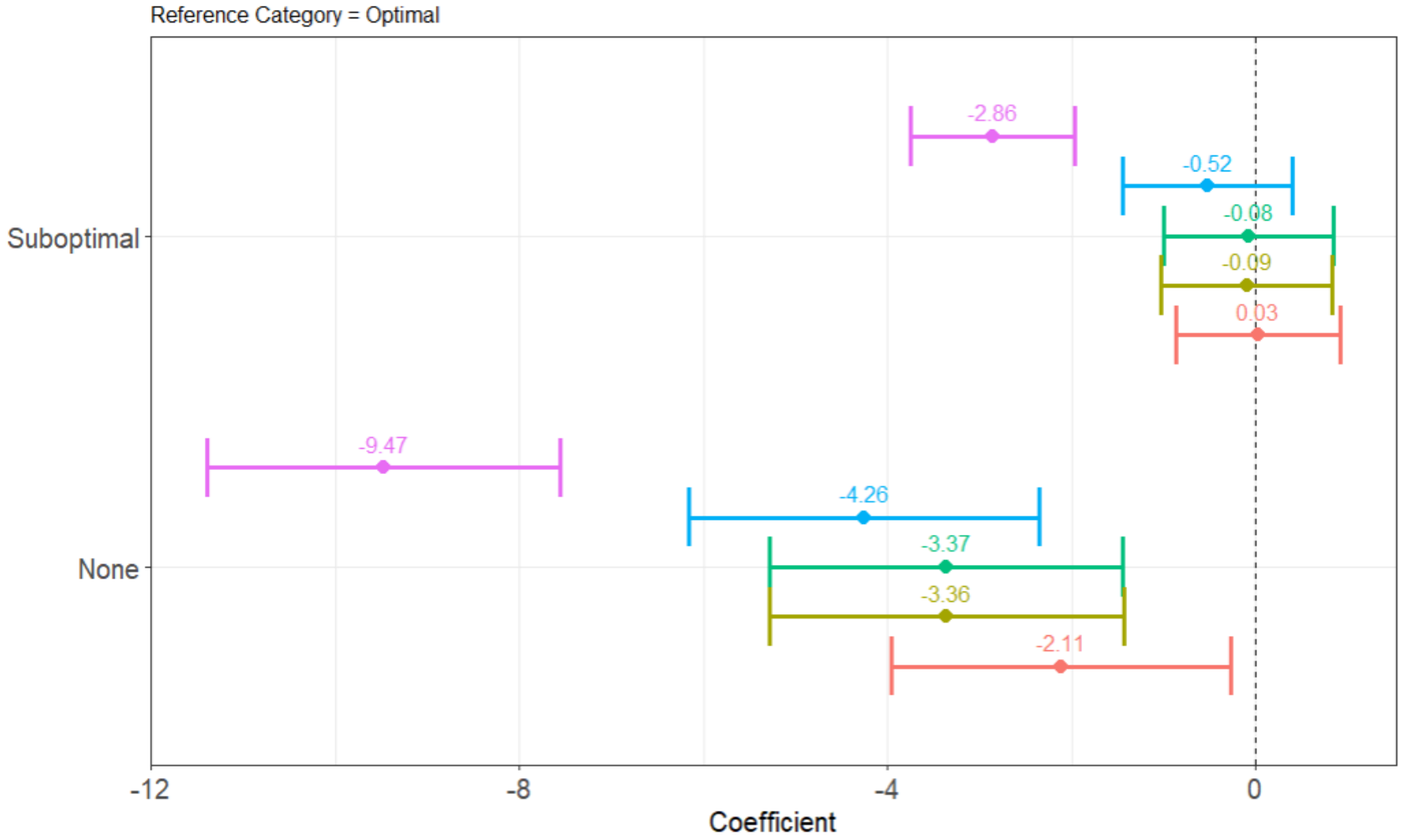
Model	Covariates	Adj.R^2	AIC
Model 1	Infant Sex	1.7%	72821
Model 2	Model 1 + Maternal Demographics	4.0%	72625
Model 3	Model 2 + Maternal Health & Obstetrics	4.4%	72588
Model 4	Model 3 + Medication & Substances	4.5%	72587
Model 5	Model 4 + Infant Details	5.5%	72507

Picture Similarities Age 5 (n=8077)



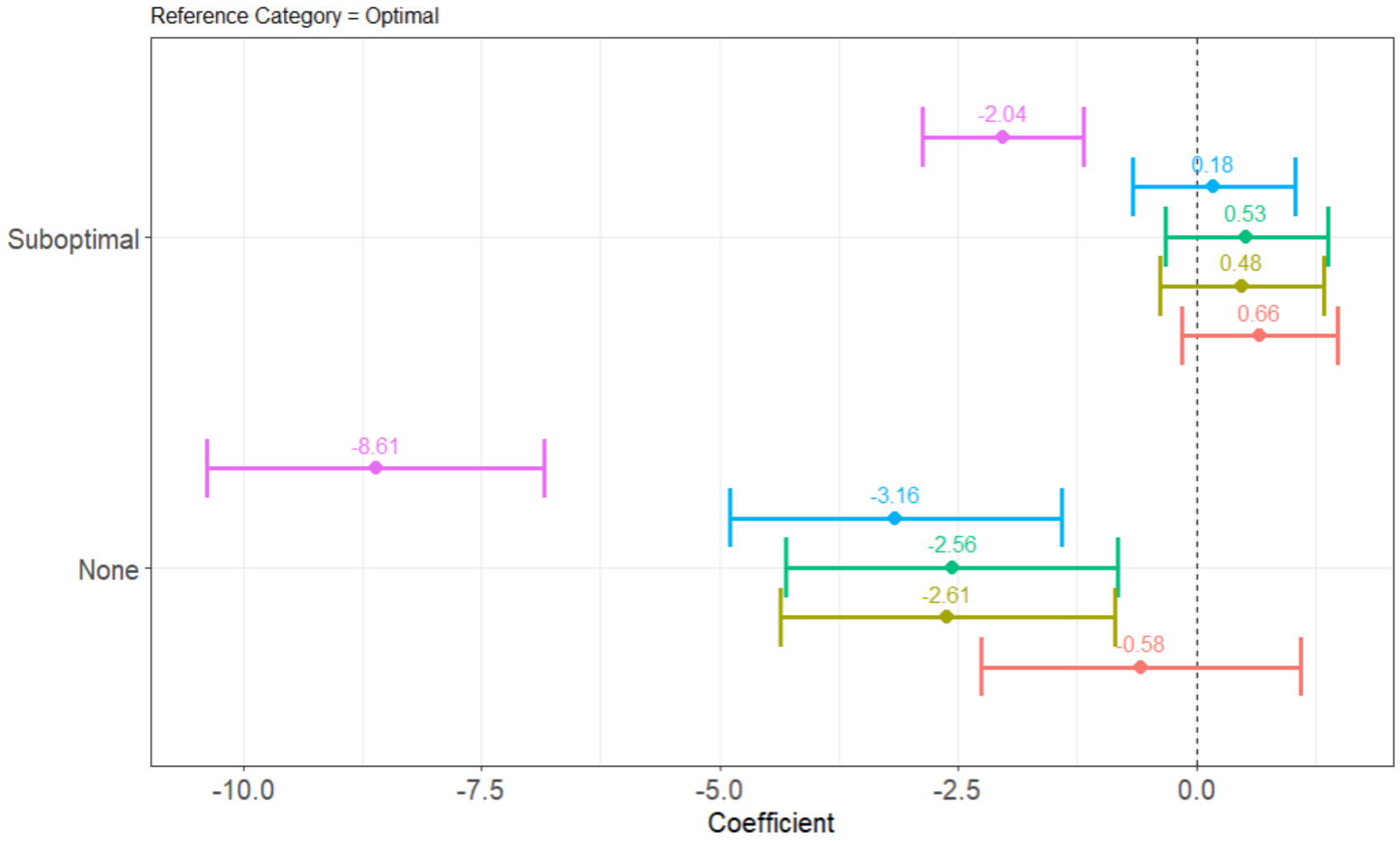
Model	Covariates	Adj.R^2	AIC
Model 1	Infant Sex	0.5%	62400
Model 2	Model 1 + Maternal Demographics	1.8%	62306
Model 3	Model 2 + Maternal Health & Obstetrics	1.9%	62299
Model 4	Model 3 + Medication & Substances	2.0%	62302
Model 5	Model 3 + Infant Details	2.4%	62275

Naming Vocabulary Age 3 (n=8647)



Model	Covariates	Adj.R^2	AIC
Model 1	Infant Sex	2.8%	75860
Model 2	Model 1 + Maternal Demographics	11.5%	75064
Model 3	Model 2 + Maternal Health & Obstetrics	12.2%	75000
Model 4	Model 3 + Medication & Substances	12.3%	75000
Model 5	Model 3 + Infant Details	18.7%	74344

Naming Vocabulary Age 5 (n=8046)



Model	Covariates	Adj.R^2	AIC
Model 1	Infant Sex	1.5%	68951
Model 2	Model 1 + Maternal Demographics	13.5%	67934
Model 3	Model 2 + Maternal Health & Obstetrics	13.6%	67906
Model 4	Model 3 + Medication & Substances	13.7%	67907
Model 5	Model 3 + Infant Details	21.5%	67146

Strengths and Limitations

Strengths

- Large nationally representative sample
- Availability of data on a large number of potential confounders.
- Directly assessed cognitive ability in a standardized way.
- Assessed cognitive ability at two different child ages

Limitations

- No information about folic acid supplementation later in pregnancy or folic acid dosage
- Some socio-demographic variables could not be included due to missing values.
- Recall bias could impact the accuracy of the data on maternal folic acid supplement use.
- The models only explained a small percentage of the total variation in BAS score.

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Discussion

Much **existing research** examining the influence of folic acid supplementation and child development **has looked at specific diagnoses such as ADHD or Autism** (Yu et al 2025).

There are some studies which have used **tests of cognitive development** (McNulty et al 2019).

Studies finding **a positive relationship fell** into two groups;

- **those which assessed only pre or early pregnancy** and
- **those that assessed the full pregnancy** period.

Many studies in the **pre or early pregnancy** group only assessed cognitive development **at a single age** often **very young** (<5 years) (Nishigori et al 2023).

Studies covering **the full pregnancy period** have typically assessed **children at an older age** but again **at a single age** (Veena et al 2010).

There are **studies which contradict the findings** in both groups and have found **no association** between early or full pregnancy supplementation or folate levels and child cognitive development (Yu et al 2025).

Conclusion

A significant relationship remained between maternal folic acid supplementation and child BAS ability score in the fully adjusted model for PS and NV at age 3, though the magnitude of this relationship was small.

At age 5 maternal folic acid supplementation was not associated with child cognitive ability for either of the subscales.

Further research is needed which assesses folic acid supplementation across the full pregnancy, has information about folic acid dose and assesses child development at multiple ages.

Thank You

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