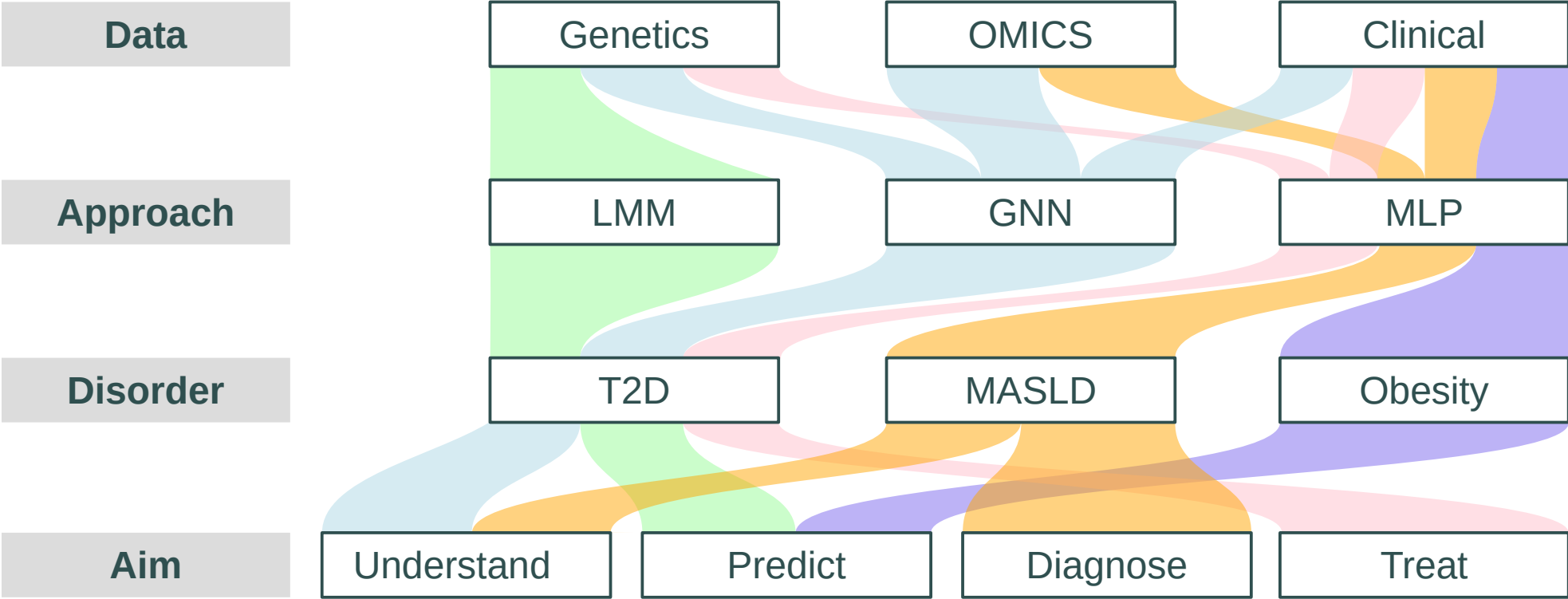
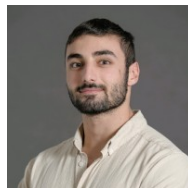


IA @ Egenodia

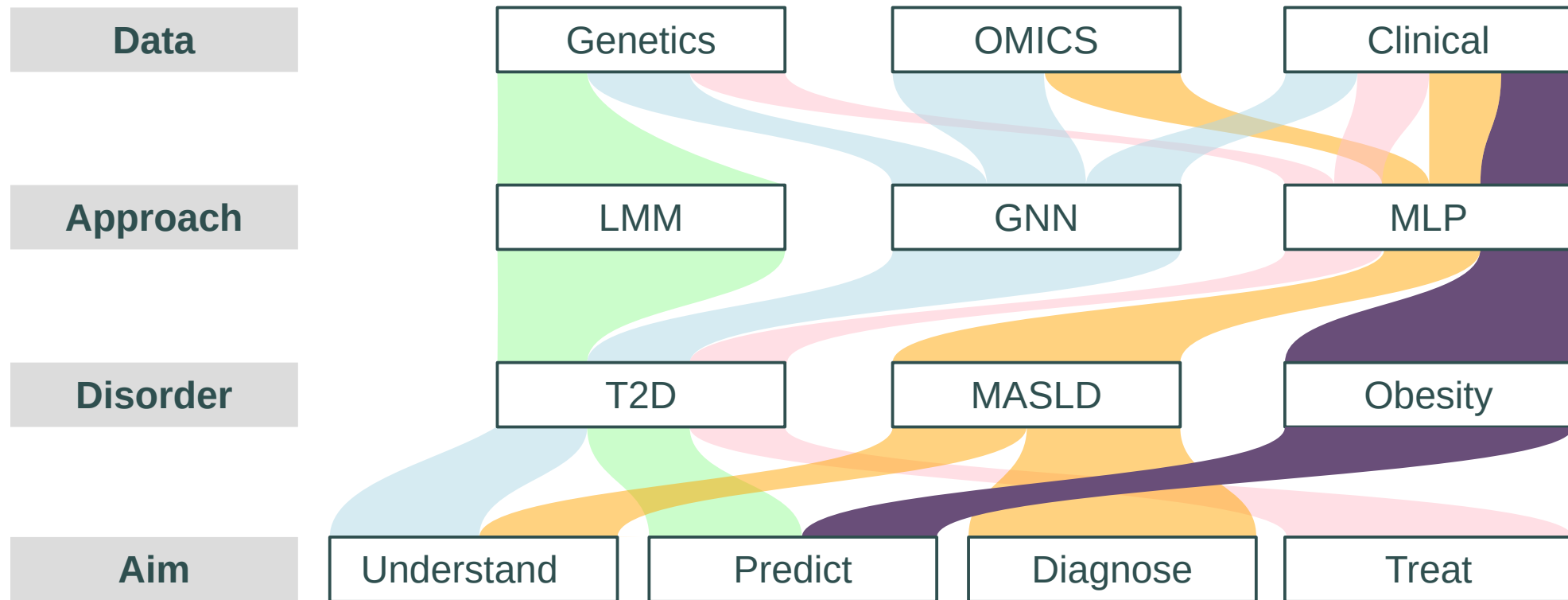


Artificial Intelligence for the precision medicine of cardiometabolic disorders





Sami Le Guilcher



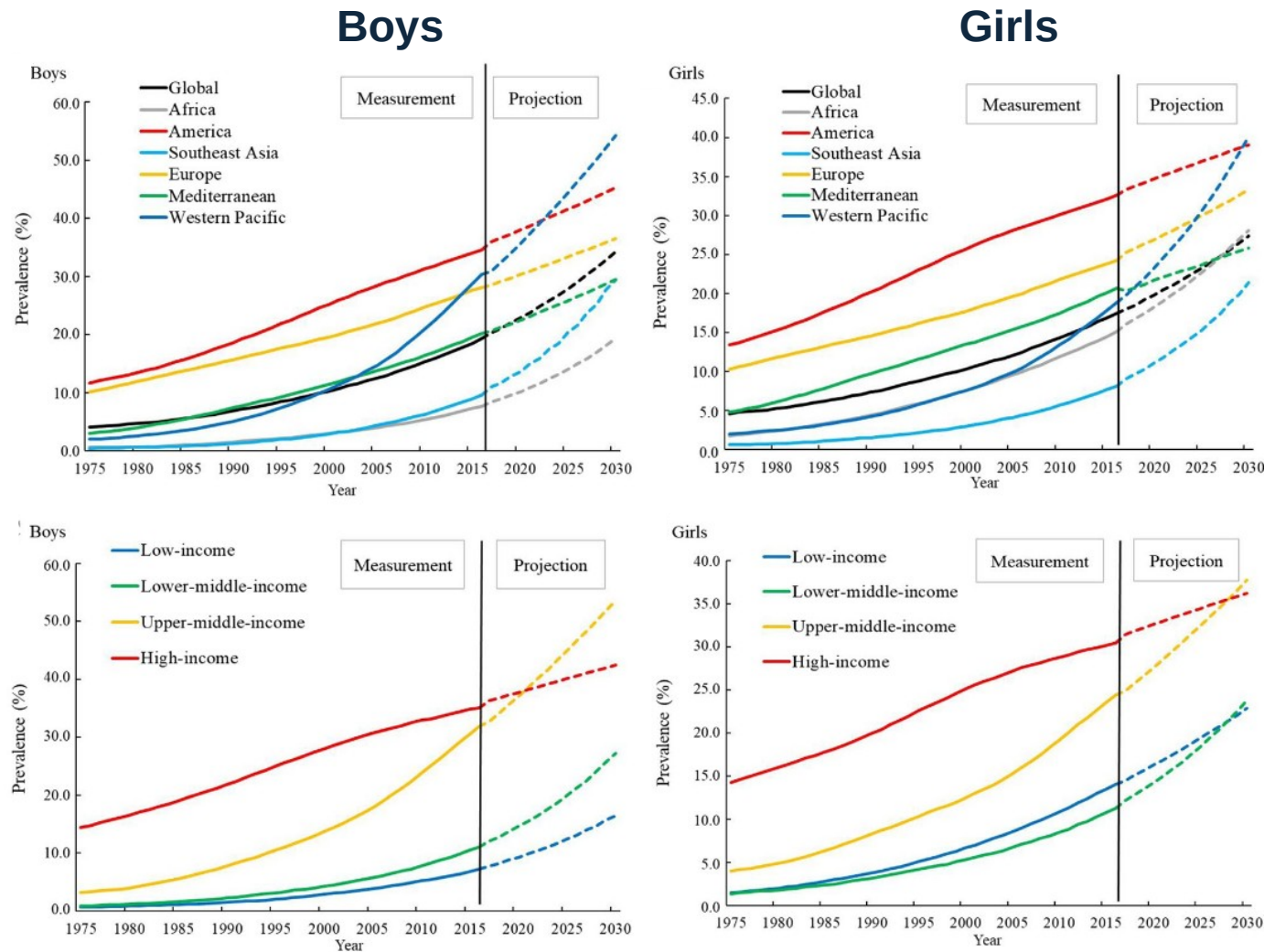
Childhood obesity, a fast growing epidemics, World

Geography

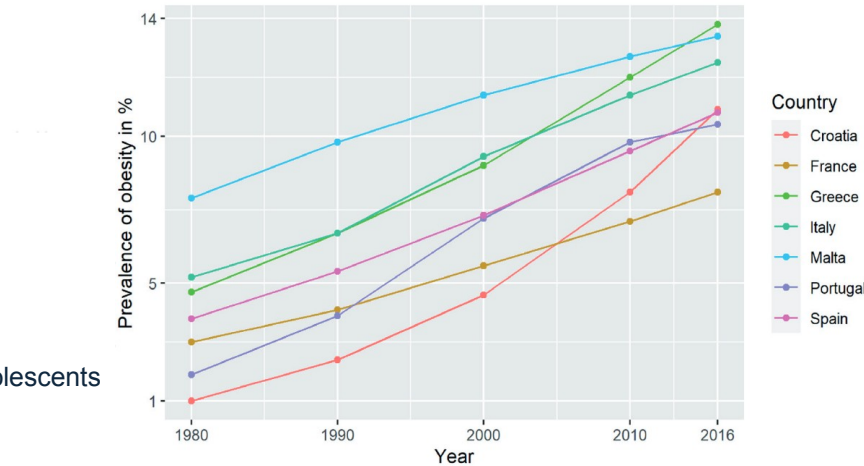
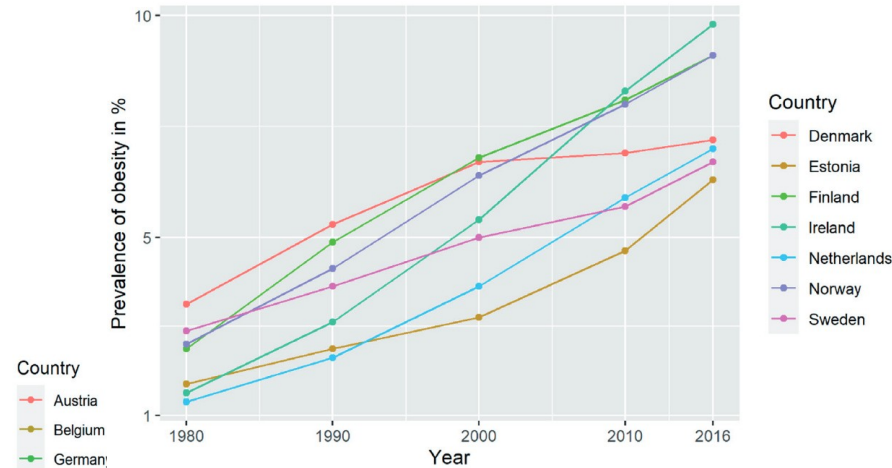
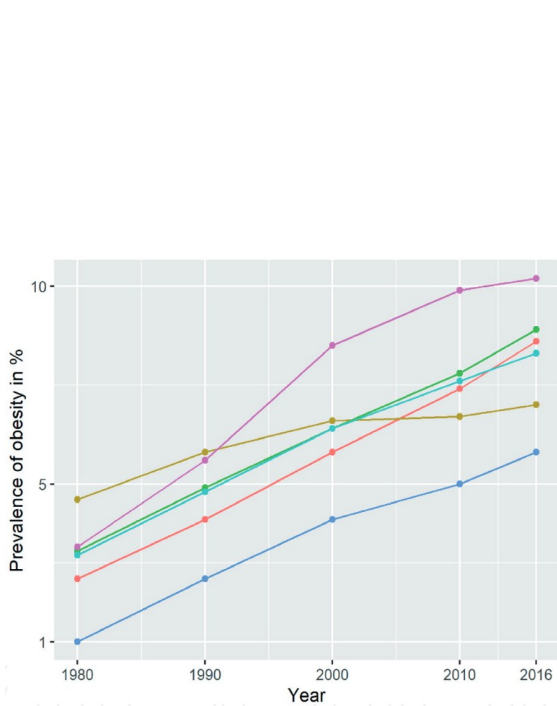
~1/3 of children
are now overweight

Income

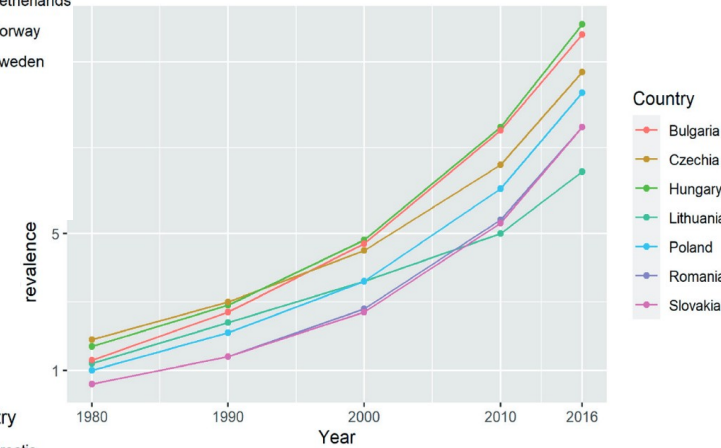
Gao *et al* (2023)
Spatial-temporal trends in global childhood
overweight and obesity from 1975 to 2030:
a weight mean center and projection analysis
of 191 countries. *Globalization and Health*, 19
<https://doi.org/10.1186/s12992-023-00954-5>



Childhood obesity, a fast growing epidemics, Europe



7-10% of European children are obese



Childhood obesity triggers health problem throughout life

In adults

- Intracranial hypertension

- Hypertension
- Dyslipidaemia
- Endothelial dysfunction
- Left ventricular hypertrophy

- Fatty liver disease

- Impaired glucose tolerance
- Polycystic ovary syndrome
- Delayed or accelerated puberty
- Metabolic syndrome
- Type 2 diabetes mellitus

- Gastro-oesophageal reflux
- Constipation
- Micronutrient deficiencies

- Coronary artery disease
- Some cancers
- Infertility
- Osteoarthritis
- Type 2 diabetes mellitus
- Adult obesity



- Reduced self esteem
- Depression
- Anxiety
- Disordered eating
- Internalizing disorders
- Body dissatisfaction



- Periodontal disease, caries

- Acanthosis nigricans, psoriasis

- Asthma
- Obstructive sleep apnoea
- Impaired exercise tolerance
- Sleep disordered breathing
- Sleep disorders
- Poor outcomes of viral infection
- Hypoventilation syndrome

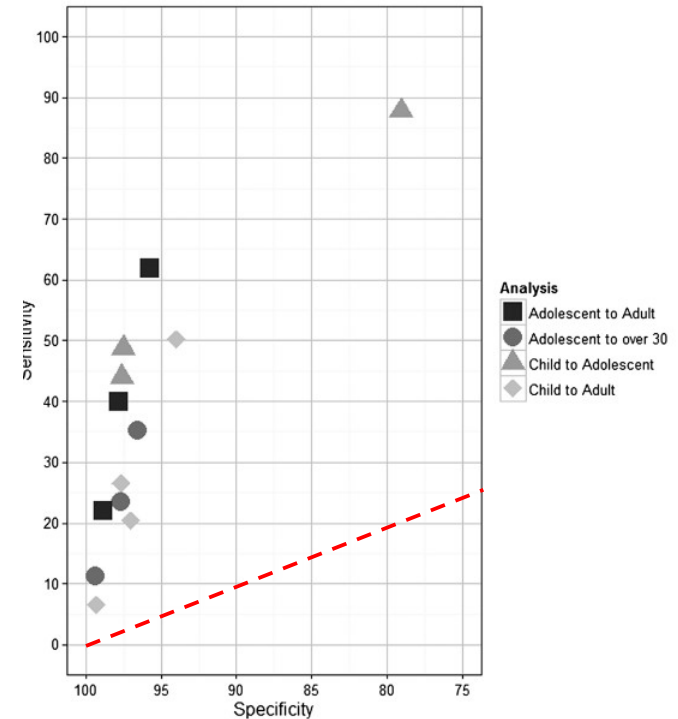
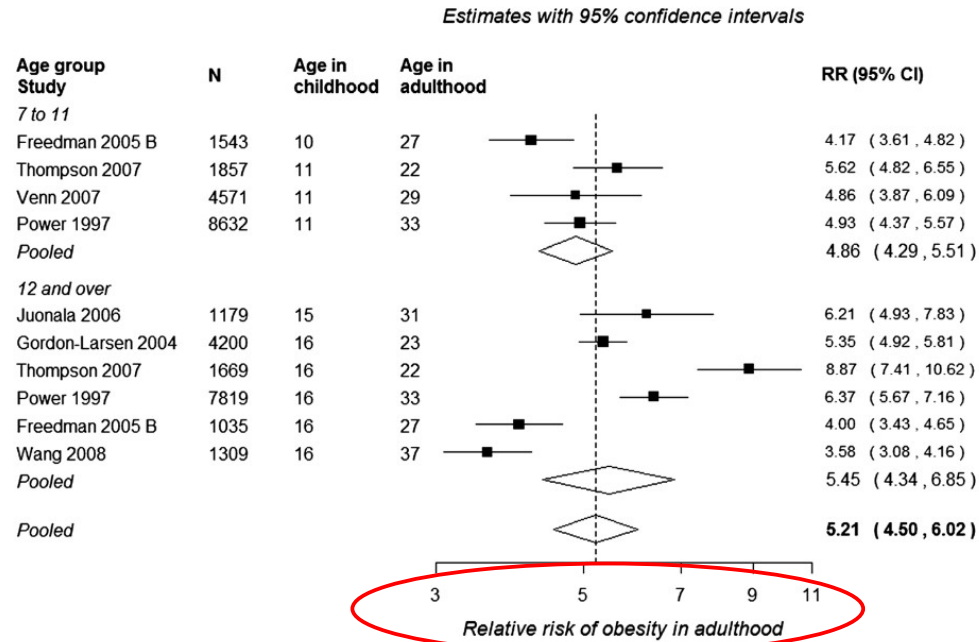
- Glomerulosclerosis, enuresis

- Pain
- Acute injuries
- Impaired balance and coordination
- Impaired muscle strength
- Gait deviations
- Postural malalignment
- Fractures
- Slipped capital femoral epiphysis
- Blount disease

- Impaired motor skill and competency
- Fatigue
- Impaired functional mobility
- Reduced health-related quality of life
- Reduced moderate-vigorous physical activity level



Childhood obesity as a predictor of adult obesity





FIGHTING CHILDHOOD OBESITY TO STAY HEALTHY ALL OVER THE LIFE (OBELISK)



Obelisk has received funding from the European Union's Horizon Europe Research and Innovation Programme under grant agreement 101080465. UK participant in Horizon Europe Project Obelisk is supported by UKRI grant number 10077650 (Beta Technology). This work is further supported by the Swiss State Secretariat for Education, Research and Innovation (SERI) under contract number 23.00160.

Obelisk Project Impacts



Increase the implementation of successful preventive and treatment programs in clinics and communities.



Decrease the rates of childhood obesity across the EU.



Increase the percentage of children and adolescents with obesity who successfully receive treatment and recover from obesity before adulthood.



Throughout their lives, children and adolescents with obesity experience improved health and a higher quality of life.

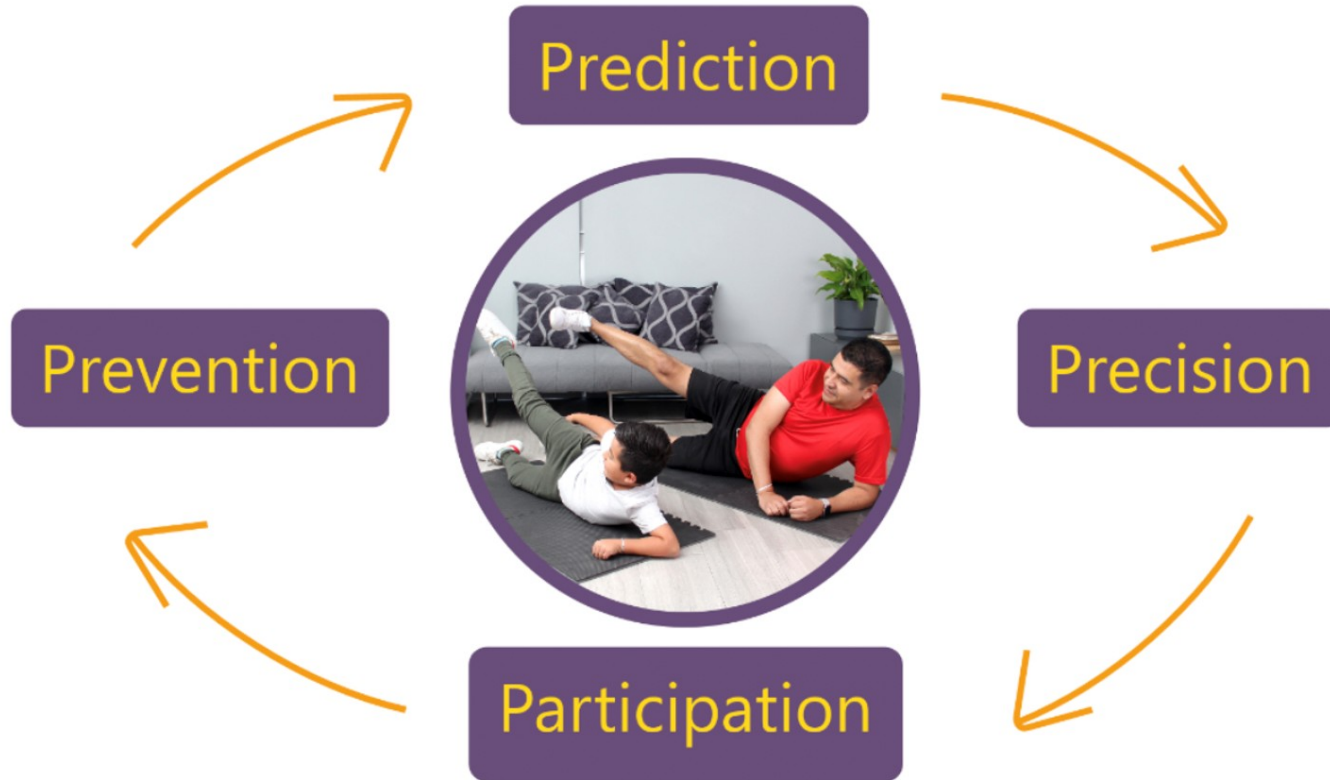


Families of children at risk for obesity or already have obesity can benefit from reduced economic burden through preventative measures and treatment options.



The evaluation of semaglutide in real-life scenarios may lead to the development of promising new medications, including dual GIP/GLP1 receptor agonists, for common types of early-onset obesity accompanied by appetite dysregulation.

WP5 4P strategies for children with obesity

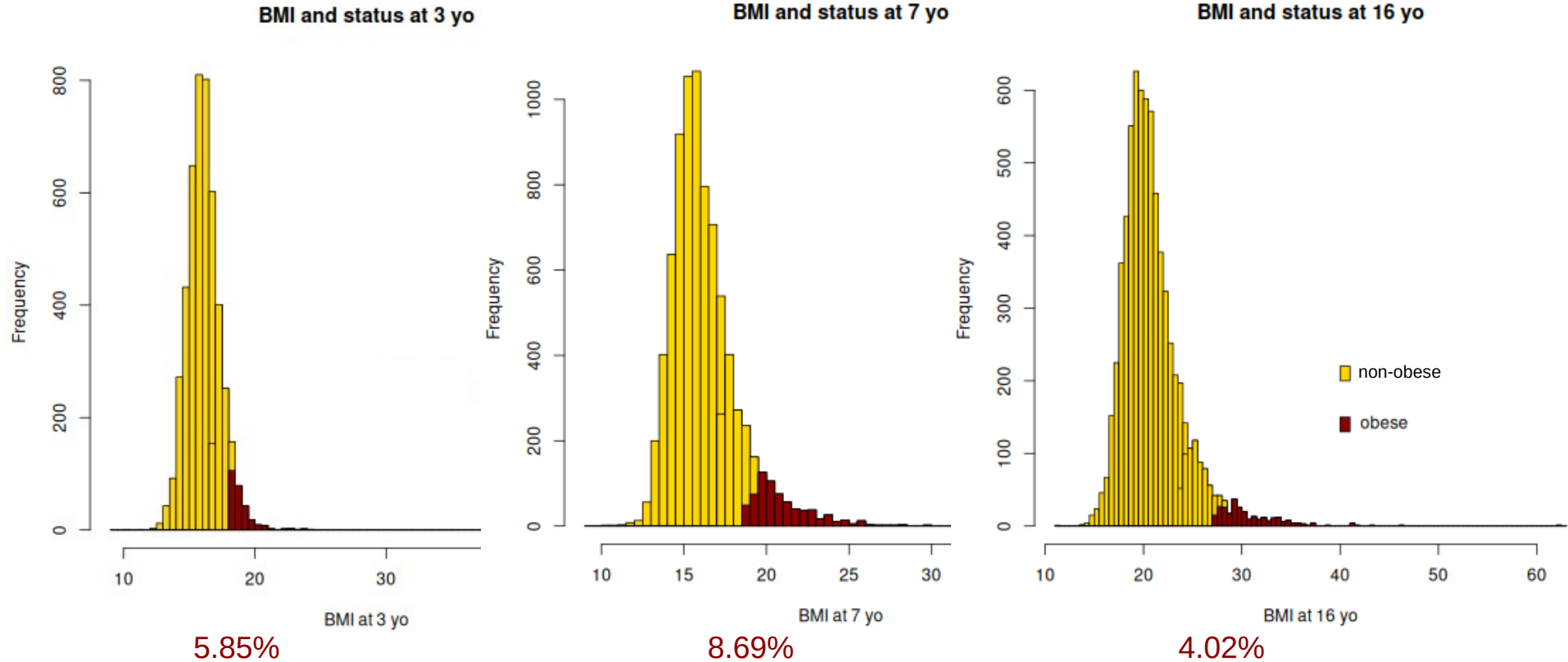


WP1 Cohorts & Trajectories

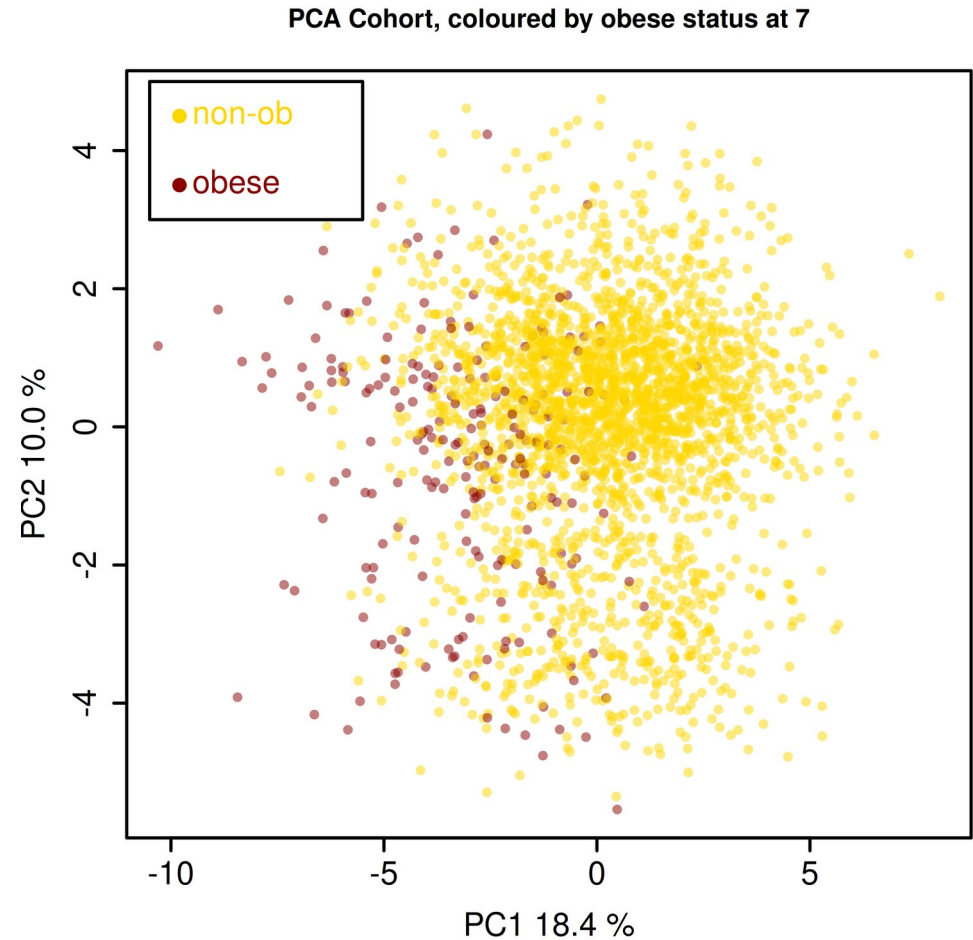
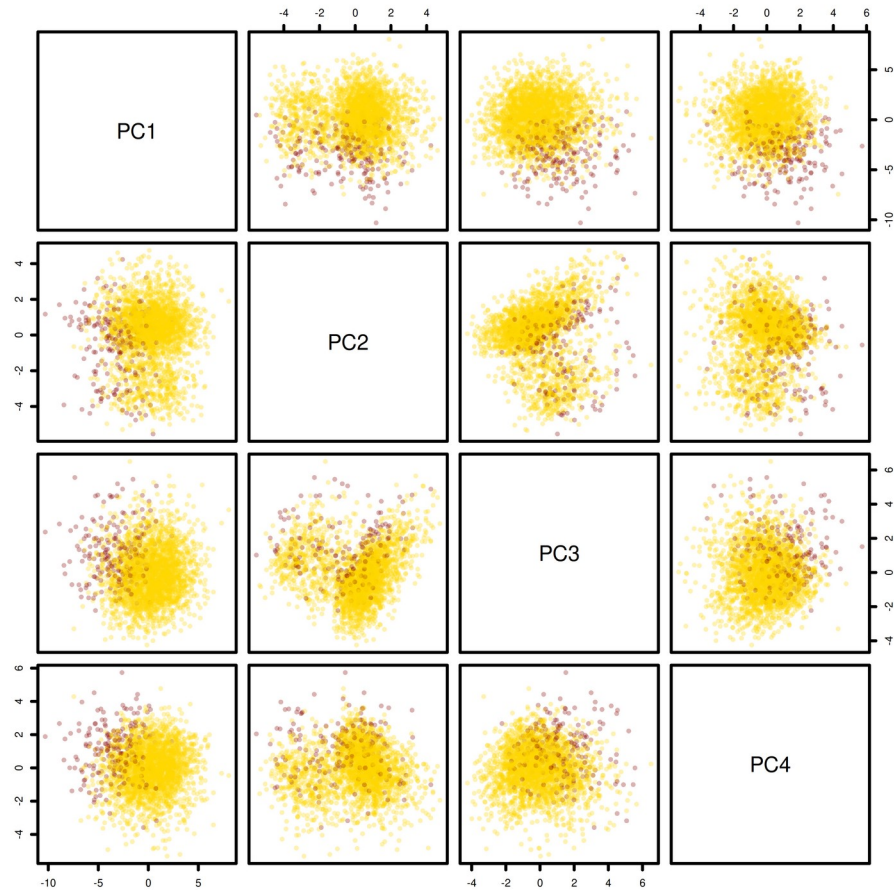
- To enrich an ongoing catalogue of FAIR data on children and their parents
- To define and explore the trajectories of childhood obesity
- To model and evaluate the burden of childhood obesity trajectories

Country	Cohort
Denmark	TOPS
Denmark	Offspring of Mother With GDM
EU	EU Child Cohort Network ((ALSPAC, Generation R, EDEN, Picolipiù)
Finland	Northern Finland Birth Cohort 1966
Finland	Northern Finland Birth Cohort 1986
Finland	Finnish Gestational Diabetes study
France	French cohort on rare obesity
France	GOOD
France	ELIPSE
Italy	PRECI.MED-VR (Obesity)
Italy	Childhood obesity group- Messina

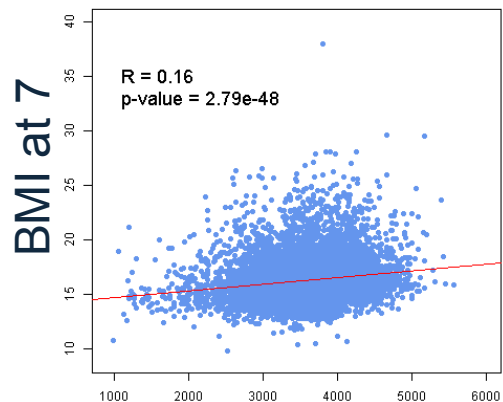
The Finn youth population was reasonably fit



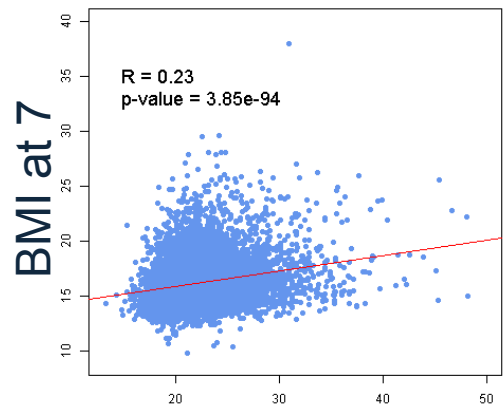
Obese vs non-obese differ but clusters are not well defined



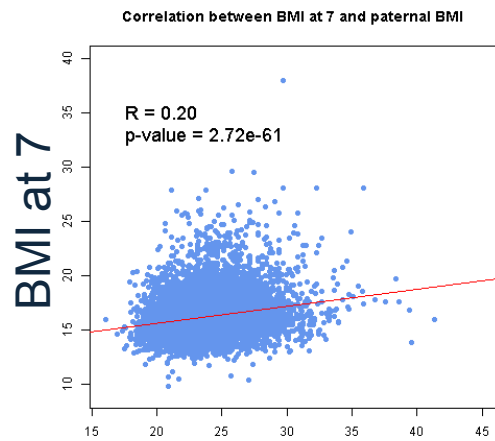
Few quantitative variables clearly correlate with obesity



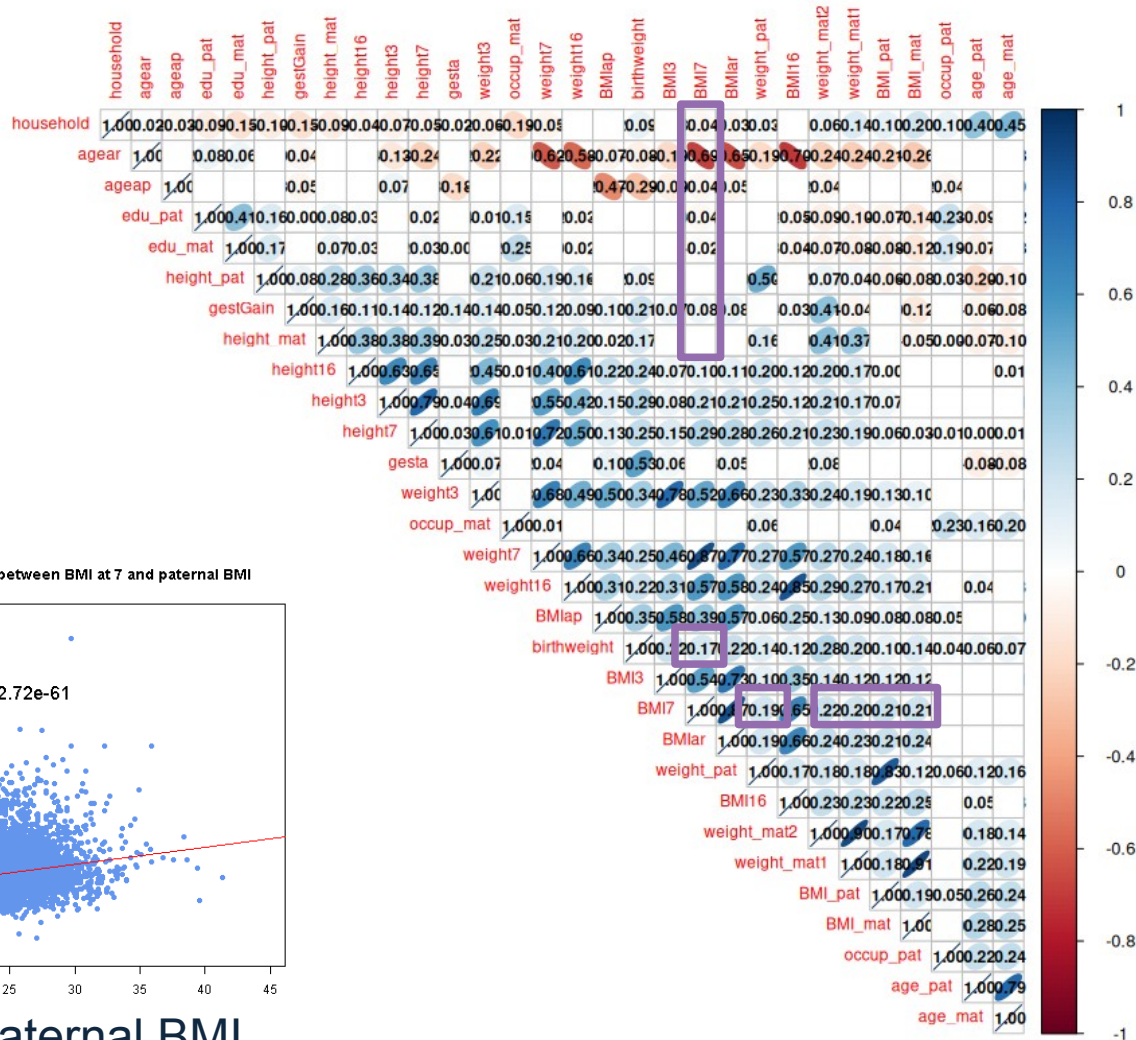
Birth weight



Maternal BMI



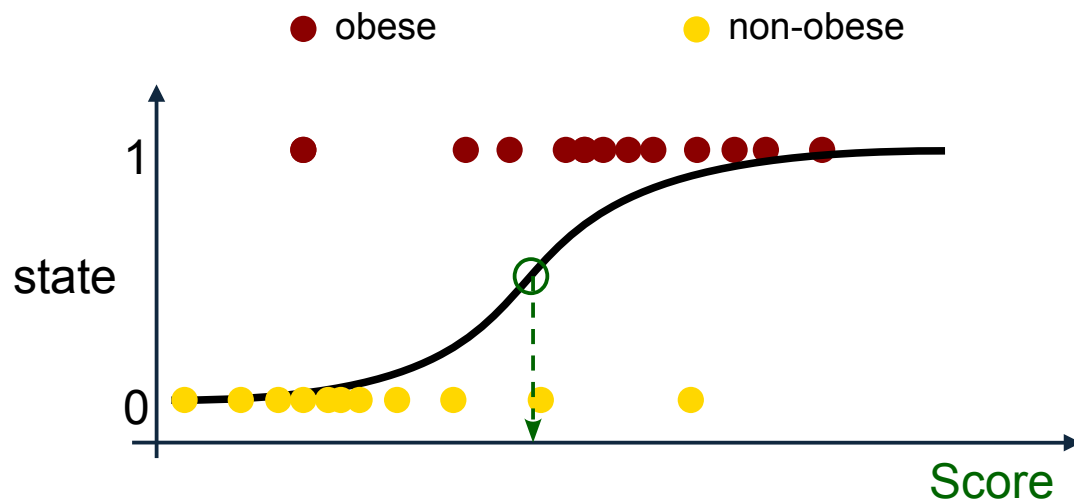
Paternal BMI



SOA: Morandi et al 2012, biological and socioeconomic variables

$$p(X) = \frac{1}{1 + e^{-(\beta_0 + \beta_1 V_1 + \beta_2 V_2 + \dots)}}$$

linear
regression

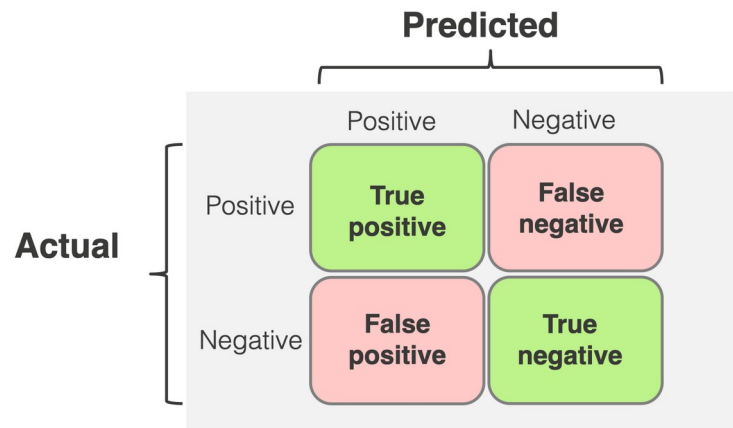


NFBC 1986:

$$\text{Risk for childhood obesity} = \frac{e^{(-10.61 + 0.12 \cdot \text{maternal BMI} + 0.18 \cdot \text{paternal BMI} - 0.31 \cdot \text{number of household members} - 0.69 \cdot \text{maternal occupation} + 0.61 \cdot \text{gestational smoking}^* + 0.75 \cdot \text{birth weight})}}{(1 + e^{(-10.61 + 0.12 \cdot \text{maternal BMI} + 0.18 \cdot \text{paternal BMI} - 0.31 \cdot \text{number of household members} - 0.69 \cdot \text{maternal occupation} + 0.61 \cdot \text{gestational smoking}^* + 0.75 \cdot \text{birth weight})})}$$

Morandi A, Meyre D, Lobbens S, Kleinman K, Kaakinen M, Rifas-Shiman SL, Vatin V, Gaget S, Pouta A, Hartikainen AL, Laitinen J, Ruukonen A, Das S, Khan AA, Elliott P, Maffei C, Gillman MW, Järvelin MR, Froguel P (2012) Estimation of Newborn Risk for Child or Adolescent Obesity: Lessons from Longitudinal Birth Cohorts. *PLoS ONE* 7(11): e49919. <https://doi.org/10.1371/journal.pone.0049919>

Evaluating a model's performance



$$\text{Accuracy} = (\text{TP} + \text{TN}) / (\text{TP} + \text{FN} + \text{TN} + \text{FP})$$

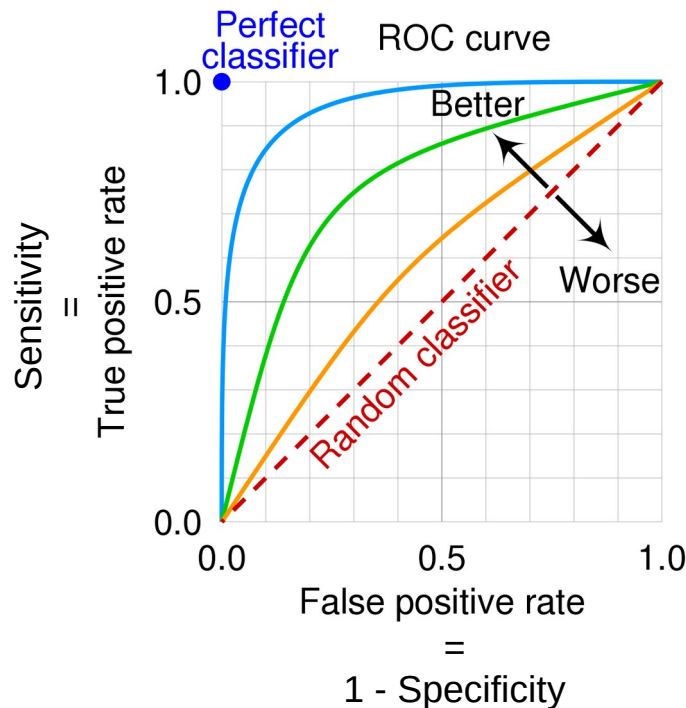
$$\text{Sensitivity (true positive rate)} = \text{TP} / (\text{TP} + \text{FN})$$

"Can we predict all obese kids?"

$$\text{Specificity (true negative rate)} = \text{TN} / (\text{TN} + \text{FP})$$

"Can we avoid wrongly predicting obesity?"

Receiver operating characteristic (ROC) curve:
performance ~ Area Under the Curve (AUC)



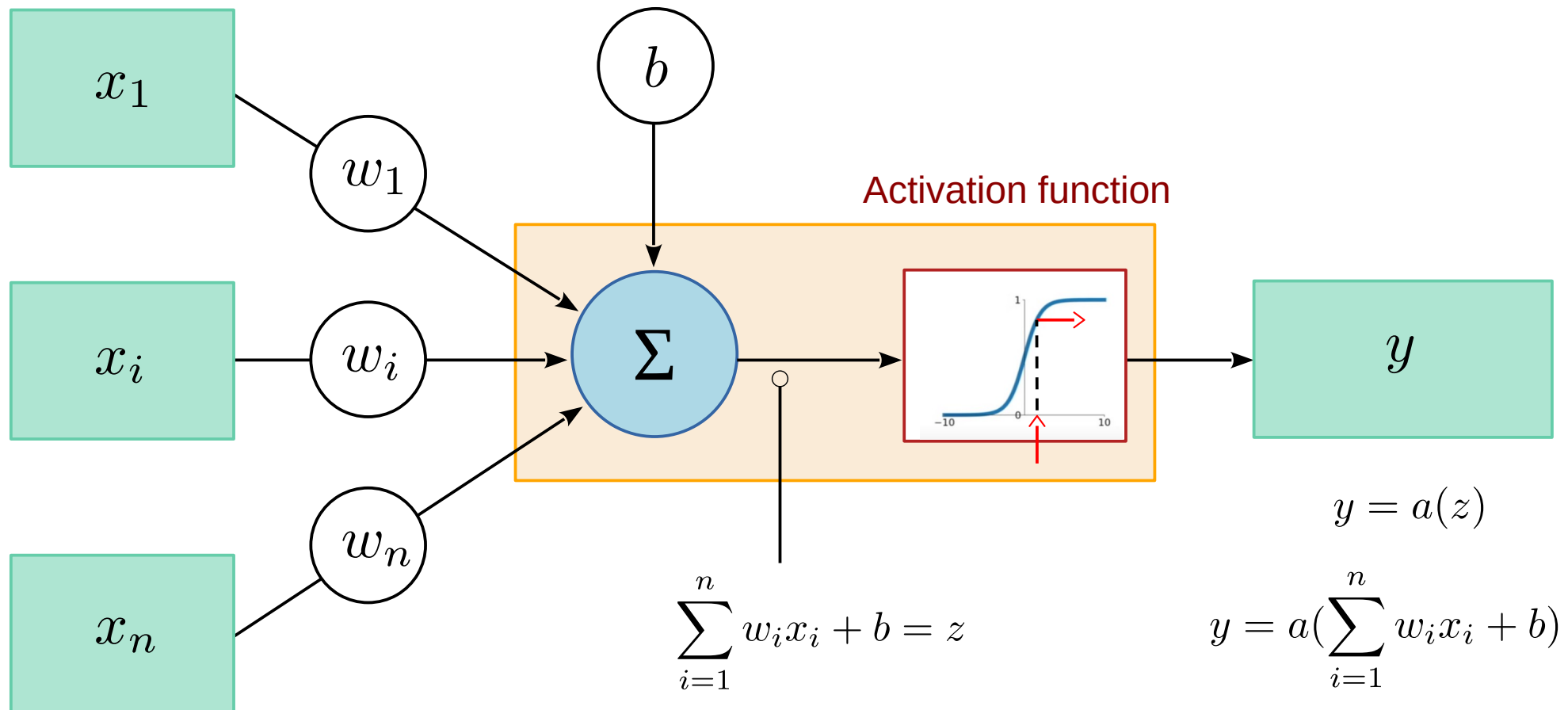
SOA: Morandi *et al* 2012, biological and socioeconomic variables

	AUROC when term is added
<i>Childhood Overweight-Obesity</i>	
Maternal BMI	0.63 (0.60–0.65)
Paternal BMI	0.65 (0.62–0.67)
N of household members	0.66 (0.64–0.68)
Gestational weight gain	0.66 (0.64–0.69)
Birth weight	0.67 (0.65–0.69)
Maternal smoking	0.67 (0.65–0.69)

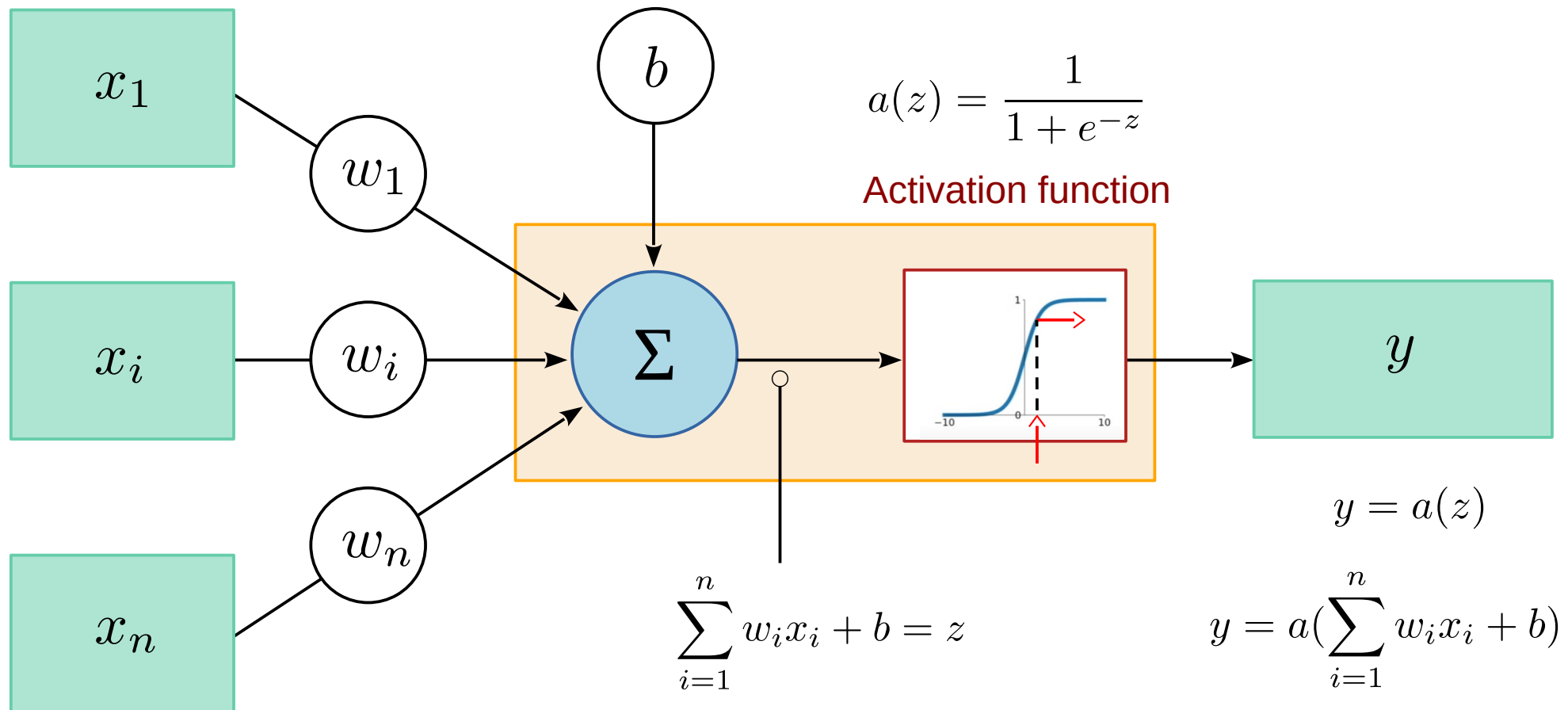
	AUROC when term is added
<i>Childhood Obesity</i>	
Paternal BMI	0.68 (0.64–0.73)
Maternal BMI	0.74 (0.70–0.78)
N of household members	0.77 (0.73–0.80)
Birth weight (kg)	0.77 (0.73–0.80)
Maternal occupation	0.77 (0.73–0.81)
Gestational smoking	0.78 (0.74–0.82)

Morandi A, Meyre D, Lobbens S, Kleinman K, Kaakinen M, Rifas-Shiman SL, Vatin V, Gaget S, Pouta A, Hartikainen AL, Laitinen J, Ruukonen A, Das S, Khan AA, Elliott P, Maffei C, Gillman MW, Järvelin MR, Froguel P (2012) Estimation of Newborn Risk for Child or Adolescent Obesity: Lessons from Longitudinal Birth Cohorts. *PLoS ONE* 7(11): e49919. <https://doi.org/10.1371/journal.pone.0049919>

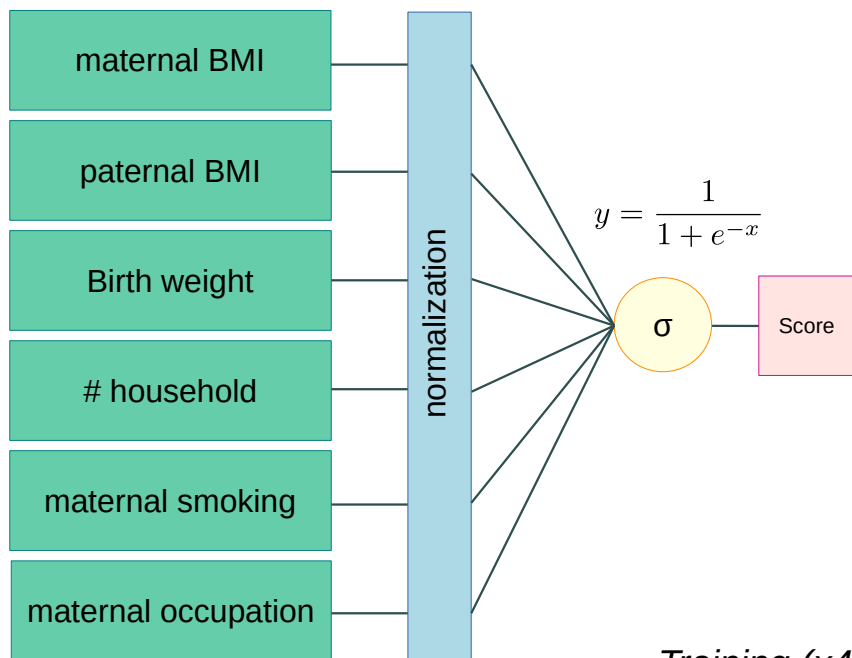
The artificial neuron



logistic regression $\approx$ 1 artificial neuron



Let's retrain Morandi



NB:

Maternal occupation

1 = unskilled/apprentice/unemployed

2 = skilled manual

3 = skilled non manual

4 = entrepreneur/professional

Training (x4)

290 obese

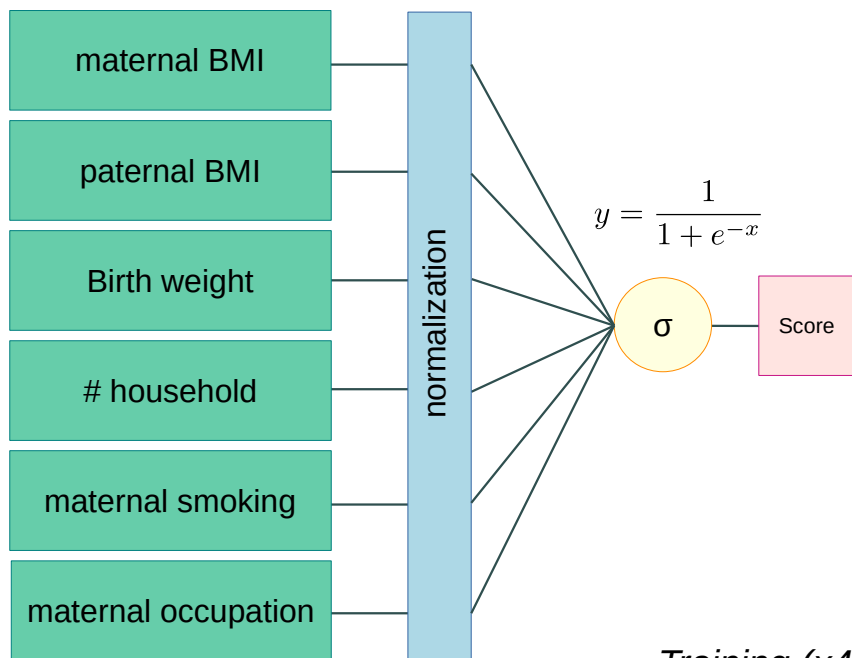
580 non-obese

Test and Validation

96 obese

192 non-obese

Let's retrain Morandi



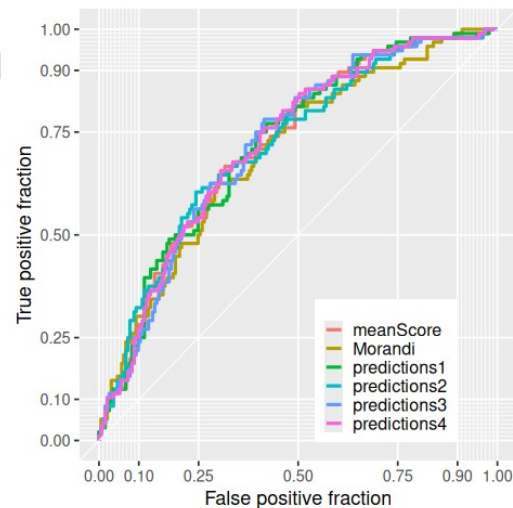
NB:
Maternal occupation
1 = unskilled/apprentice/unemployed
2 = skilled manual
3 = skilled non manual
4 = entrepreneur/professional

Training (x4)
290 obese
580 non-obese

Test and Validation
96 obese
192 non-obese

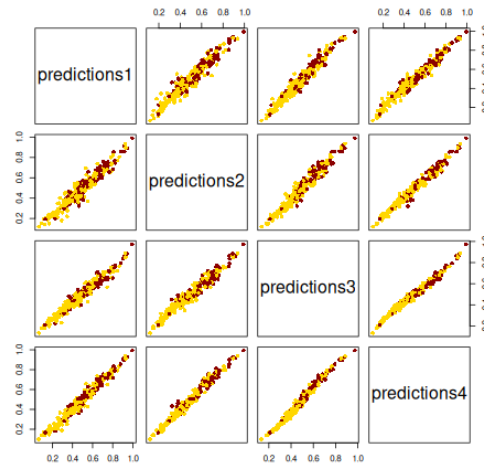
AUC
Morandi = 0.701
Now = 0.72
Sensitivity = 64.6

Validation set

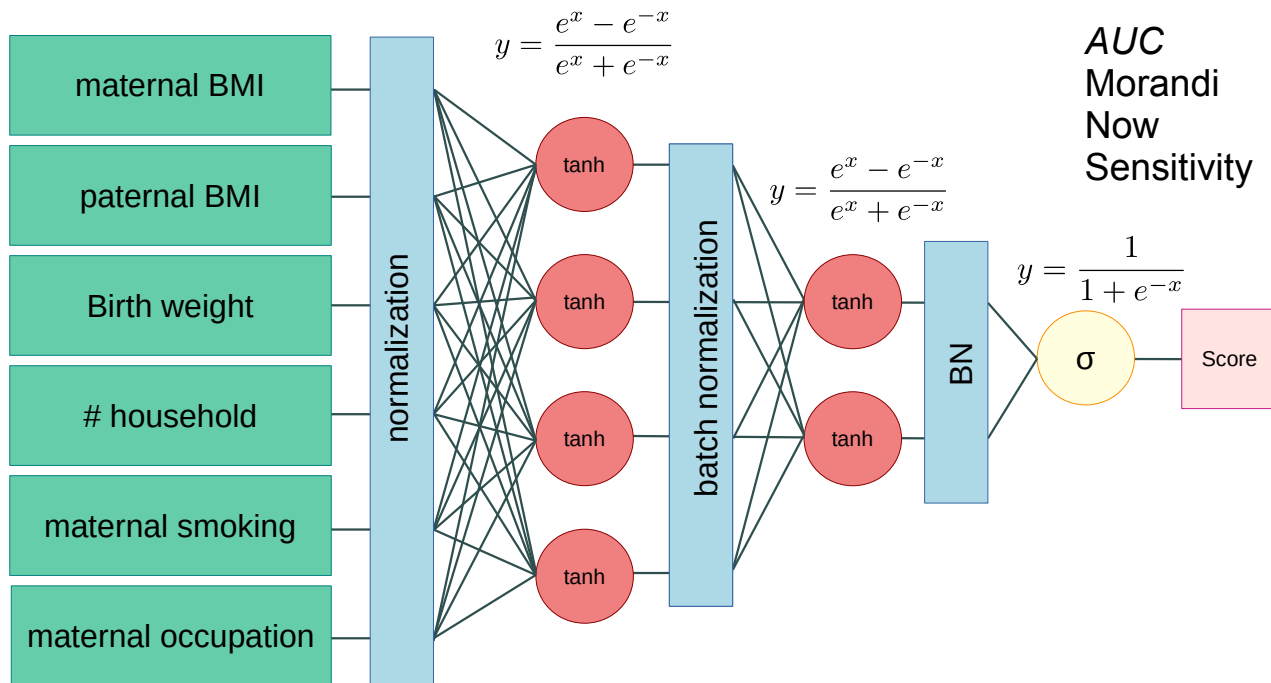


● actually obese
● actually non-obese

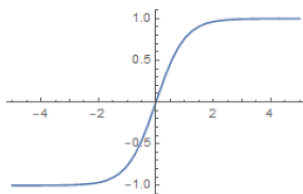
Comparison
models' scores



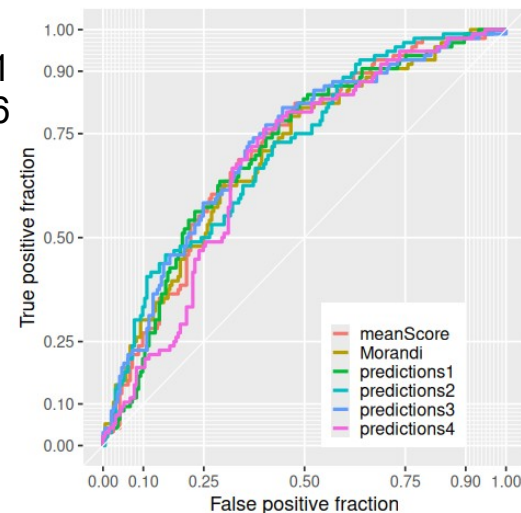
Can we improve on that?



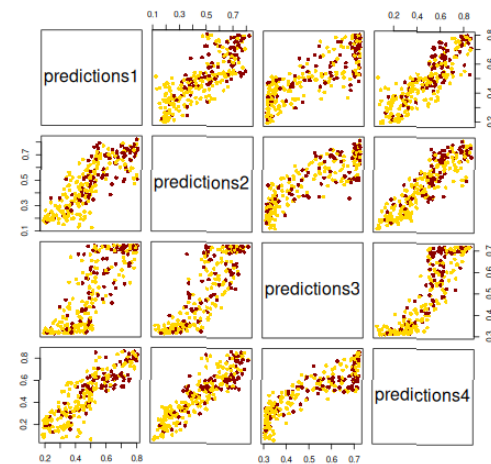
AUC
Morandi = 0.701
Now = 0.726
Sensitivity = 67.7



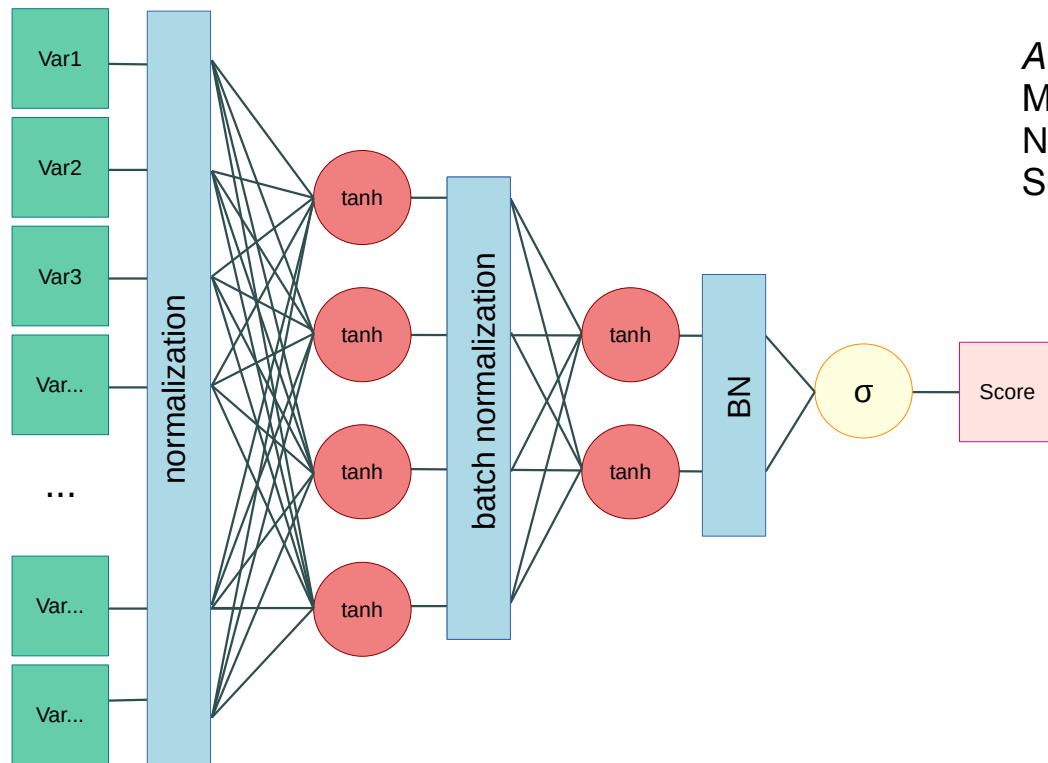
Validation set



Comparison models' scores

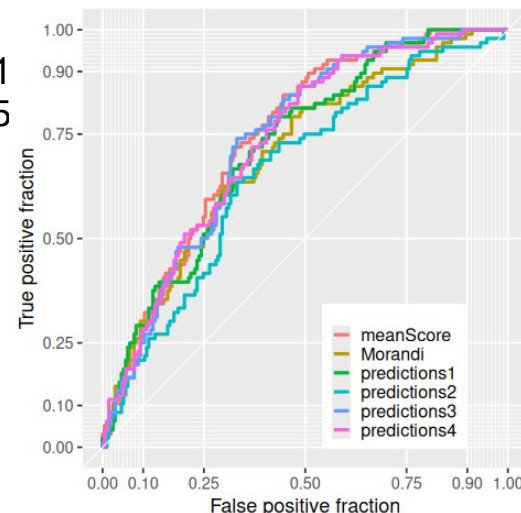


Increasing the number of variables



AUC
Morandi = 0.701
Now = 0.745
Sensitivity = 69.8

Validation set

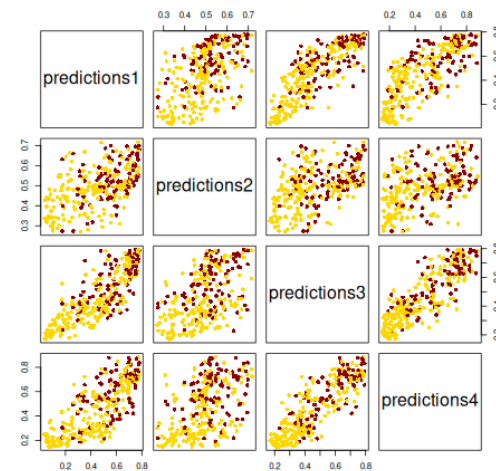


Variables =
gender, birth weight, BMI mat, BMI pat, gestational weight gain, # household, maternal smoking (2nd month), maternal and paternal alcohol, maternal and paternal education, maternal and paternal occupation



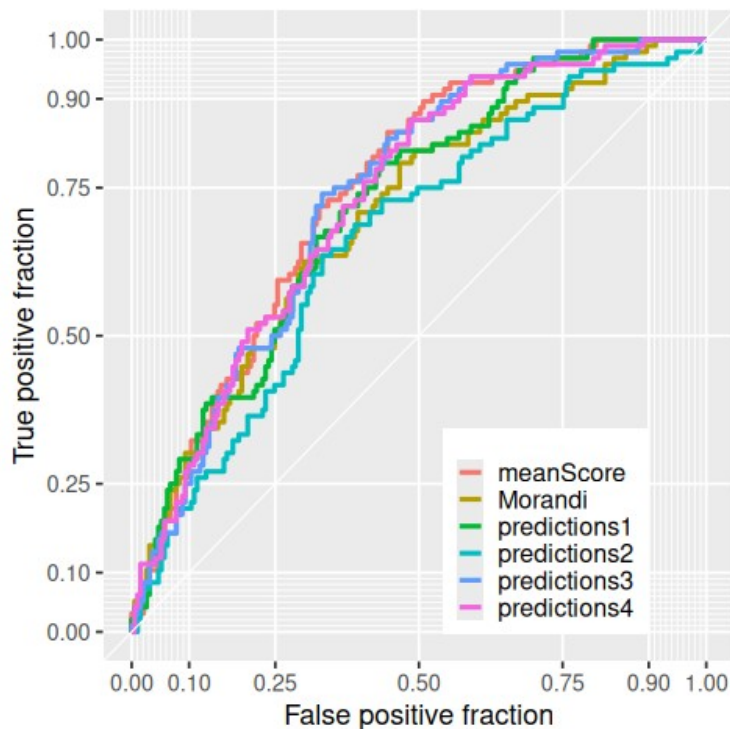
4 levels based on ISCED

Comparison models' scores



Increasing the number of variables

Validation set



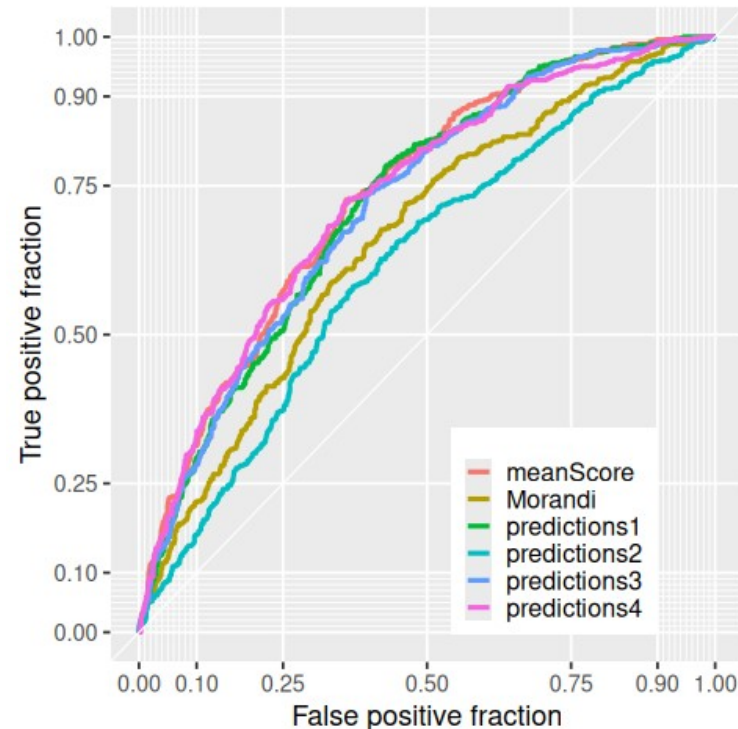
AUC

Morandi = 0.701

Now = 0.745

Sensitivity = 69.8

Entire set



AUC

Morandi = 0.661

Now = 0.73

Sensitivity = 71.4

How good is the prediction?

FP =
predicted obese,
actually non-obese

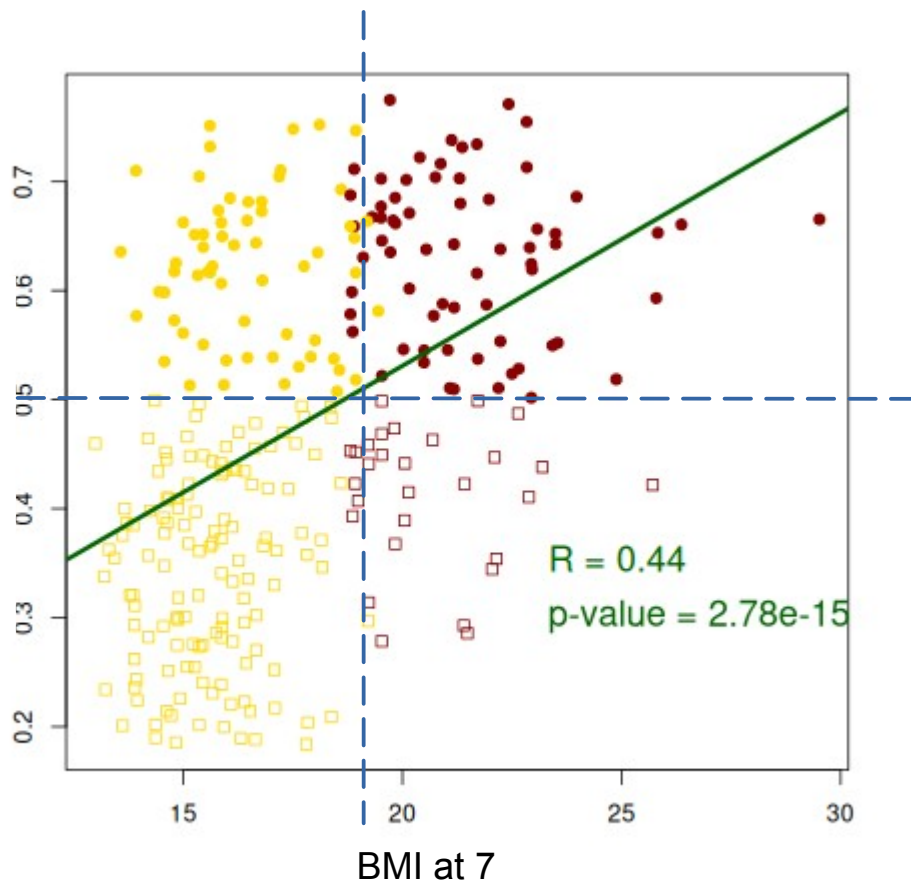
Over-zealous:
Stigmatising?

TP =
predicted obese,
actually obese

TN =
predicted non-obese,
actually non-obese

FN =
predicted non-obese,
actually obese

mean of
models' scores



mean of models' scores correlates with BMI

Missed:
Failure to duty?

Acknowledgments

The group

Smaïn Fettes
Marwa Afnouch
Omama Binan
Sami Le Guilcher
Arthur Six

The tools

R package developers
(*VIM, MICE, DESeq2, ChAMP*)

Python package developers
(*Tensorflow/Keras, Numpy, Pandas, Scikit-learn*)

Egenodia

Philippe Froguel
Amélie Bonnefond

Mathilde Boissel
Mehdi Derhourhi
Emma Henriques
Stefan Gaget
ShuangShuang Geng
Anne-Sophie Ledoux
Vincent Massy
Lijiao Ning

Hélène de Gavre
Mélanie Hocquet

Obelisk

Anita Morandi
Rozenn Nedelec
Susanna Pätsi
Sylvain Sebert

