GESTATIONAL WEIGHT GAIN STANDARDS IN NORMAL-WEIGHT WOMEN IN THE INTERGROWTH-21ST PROJECT

UNIVERSITY OF OXFORD

WHY DO WE NEED TO MONITOR GESTATIONAL WEIGHT GAIN (GWG)?

Risk factors associated with inadequate GWG

- Low birth weight
- Small-for-gestational age
- Pre-term birth
- Macrosomia
- Gestational diabetes mellitus
- Caesarean section
- Infant mortality
- Postpartum weight retention
- Childhood obesity

IOM RECOMMENDATIONS

- Recommendations for the American population
- 1990 → GWG guidelines based on Metropolitan Life Insurance BMI tables and considered the infant's welfare only
- 2009 → current guidelines based on WHO BMI classification and considers both maternal and infant's welfare
  - GWG is considered within the whole reproductive cycle framework, i.e. from pre-conception to 1 year post-partum
  - Review of available data on the various aspects linked to GWG

GWG RECOMMENDATIONS

BMI category	GWG range (kg)
Underweight (< 18.5 kg/m^2)	12.5-18
Normal weight (18.5-24.9 kg/m^2)	11.5-16
Overweight (25.0-29.9 kg/m^2)	7-11.5
Obese (≥ 30.0 kg/m^2)	5-9

IOM/NRC.Weight gain during pregnancy: re-examining the guidelines. 2009.

IOM GWG RECOMMENDATIONS

- No international consensus on GWG
- Absence of appropriate GWG guidelines or agreement on what constitutes adequate GWG due to gaps in the knowledge as identified by IOM
- Heterogeneity of the methodological quality of available studies → systematic review *(Ohadike et al. Adv Nutr, 2015 - accepted)*

IOM/NRC.Weight gain during pregnancy: re-examining the guidelines. 2009.

WHO RECOMMENDATIONS FOR THE CREATION OF GROWTH CHARTS

- Prescriptive : shows how populations should grow under optimal conditions with no known environmental constraints on growth
- Longitudinal studies of selected populations with a low incidence of maternal and fetal complications
- With regular collection of anthropometric data before, during and after pregnancy

WHO Growth Standard for children between 0-5 years of age

WHO.Technical Report Series 1995;854

DESCRIPTIVE VS. PRESCRIPTIVE CHARTS

DESCRIPTIVE

Descriptive charts describes how a population at a certain place and at a certain time grew

PRESCRIPTIVE

Prescriptive charts shows how populations should grow under optimal conditions with no known environmental constraints on growth

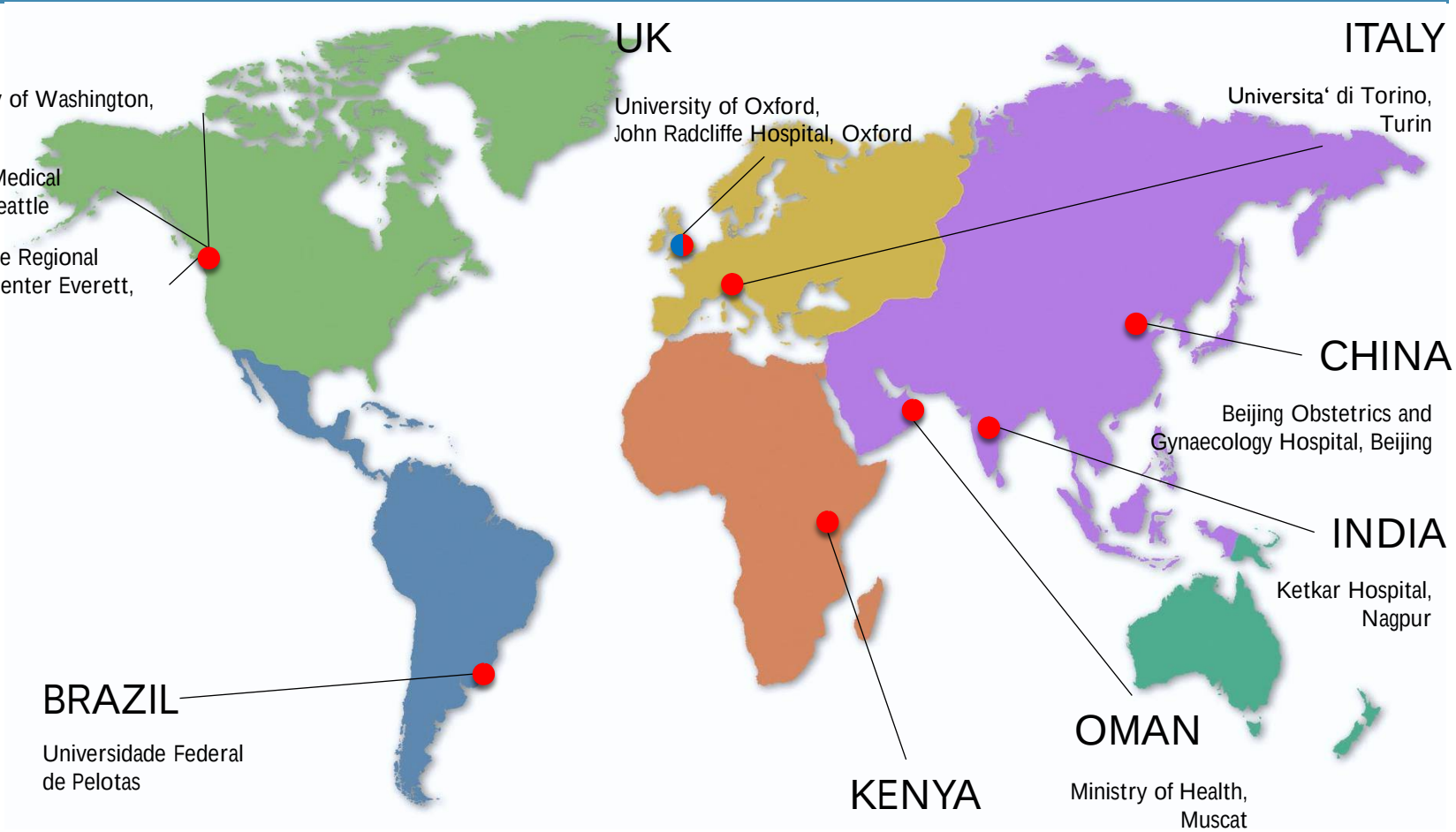
WHO.Technical Report Series 1995;854

INTERGROWTH-21ST PROJECT

INTERGROWTH-21ST PROJECT

- International large-scale, multicentre, population-based project, conducted between April 2009 and March 2014, in 8 well-demarcated urban sites
- The primary aim was to produce international standards for fetal, newborn and preterm growth using the same conceptual framework as the WHO Multicentre Growth Reference Study so as to complement the existing WHO Child Growth Standards

INTERGROWTH-21ST SITES



PROJECT STUDIES

- Longitudinal Fetal Growth Study (FGLS) designed for the purpose of constructing fetal growth standards conducted in a cohort of healthy women *[Papageorghiou et al. Lancet 2014; 384]*

- Postnatal Preterm Follow-up Study (PPFS) that closely monitored infants in the longitudinal cohort who were born prematurely *[Villar et al. Lancet Global Health (on line)]*

- Neonatal Cross-Sectional Study (NCSS) designed for the purpose of constructing newborn standards (neonatal size at birth) *[Villar et al. Lancet 2014; 384]*

OBJECTIVE

To describe GWG in healthy pregnant women from the INTERGROWTH-21st Project's FGLS with good maternal and perinatal outcomes

Only results for normal-weight women are presented

FETAL LONGITUDINAL GROWTH STUDY

- Recruitment at ≤ 14 weeks' of gestation
- Fulfilling INTERGROWTH-21st criteria for "Low-risk pregnancy"
- Baseline maternal height and weight at study entry
- Antenatal visits every 5 ± 1 weeks included weight measurements
- All study sites used the same standardised equipment and protocol *
- Cumulative GWG

** INTERGROWTH-21st Project. Anthropometry Handbook. 2012.*

LOW-RISK PREGNANCY CRITERIA

a) aged ≥18 and ≤35 years;
b) BMI ≥18.5 and <30 kg/m^2;
c) height ≥ 153 cm;
d) singleton pregnancy;
e) a known LMP with regular cycles (defined as a 26-30 day cycle in the previous 3 months), without hormonal contraceptive use, pregnancy or breastfeeding in the 3 months before pregnancy;

Criteria defining a low-risk study population as healthy and well-nourished (both before and during pregnancy) to ensure that fetal growth is optimal

n) no previous pregnancy affected by pre-eclampsia/eclampsia, HELLP syndrome or a related pregnancy-associated condition;
o) no clinically significant atypical red cell alloantibodies;
p) negative urinalysis;
q) systolic blood pressure <140 mmHg and diastolic blood pressure < 90 mmHg;
r) haemoglobin ≥11 g/dl;
s) negative syphilis test and no clinical evidence of any other sexually transmitted diseases, including clinical Trichomoniasis;
t) not in an occupation with risk of exposure to chemicals or toxic substances, or very physically demanding activity to be evaluated by local standards. Also women should not be conducting vigorous or contact sports, as well as scuba diving or similar activities

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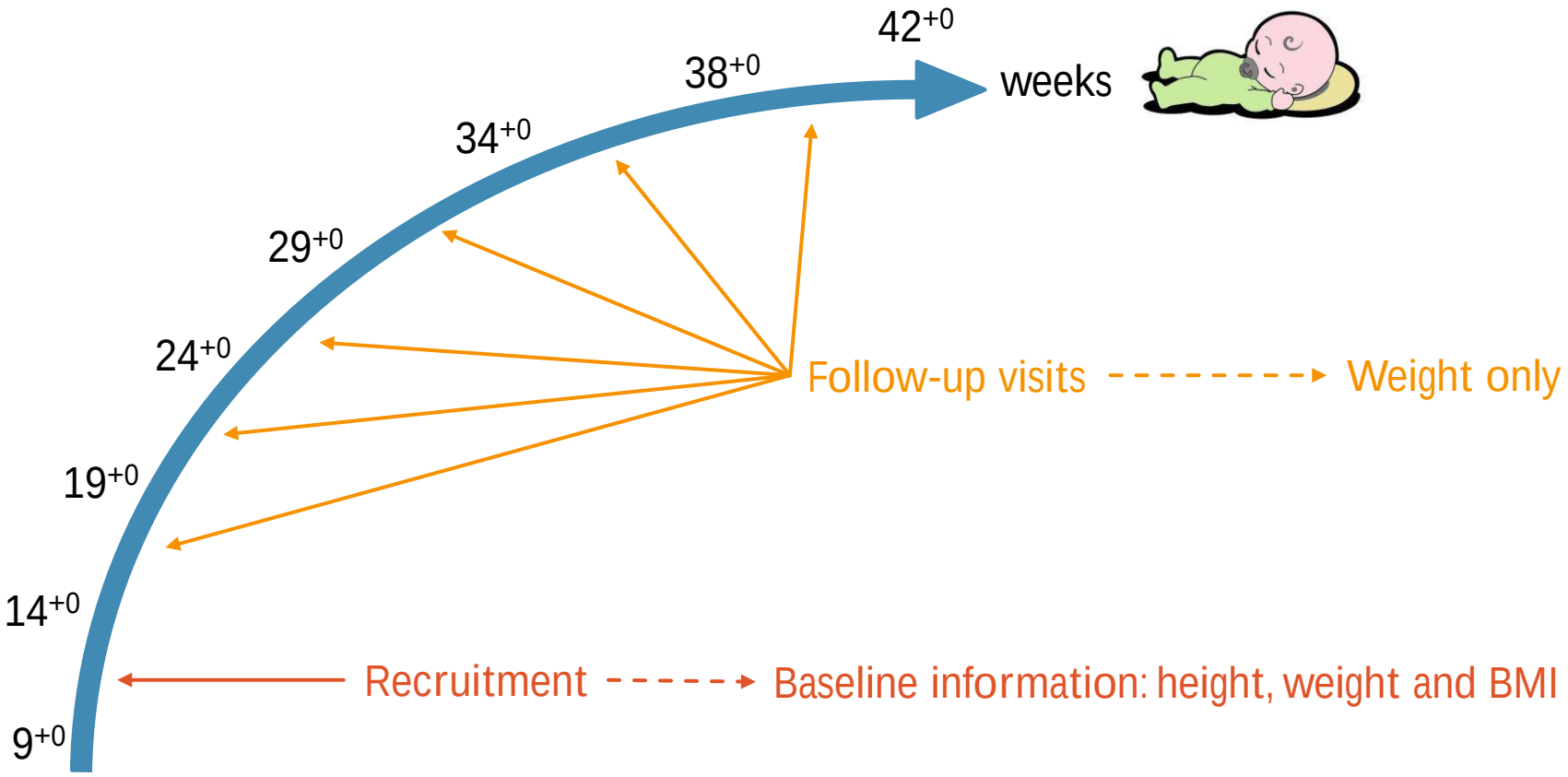
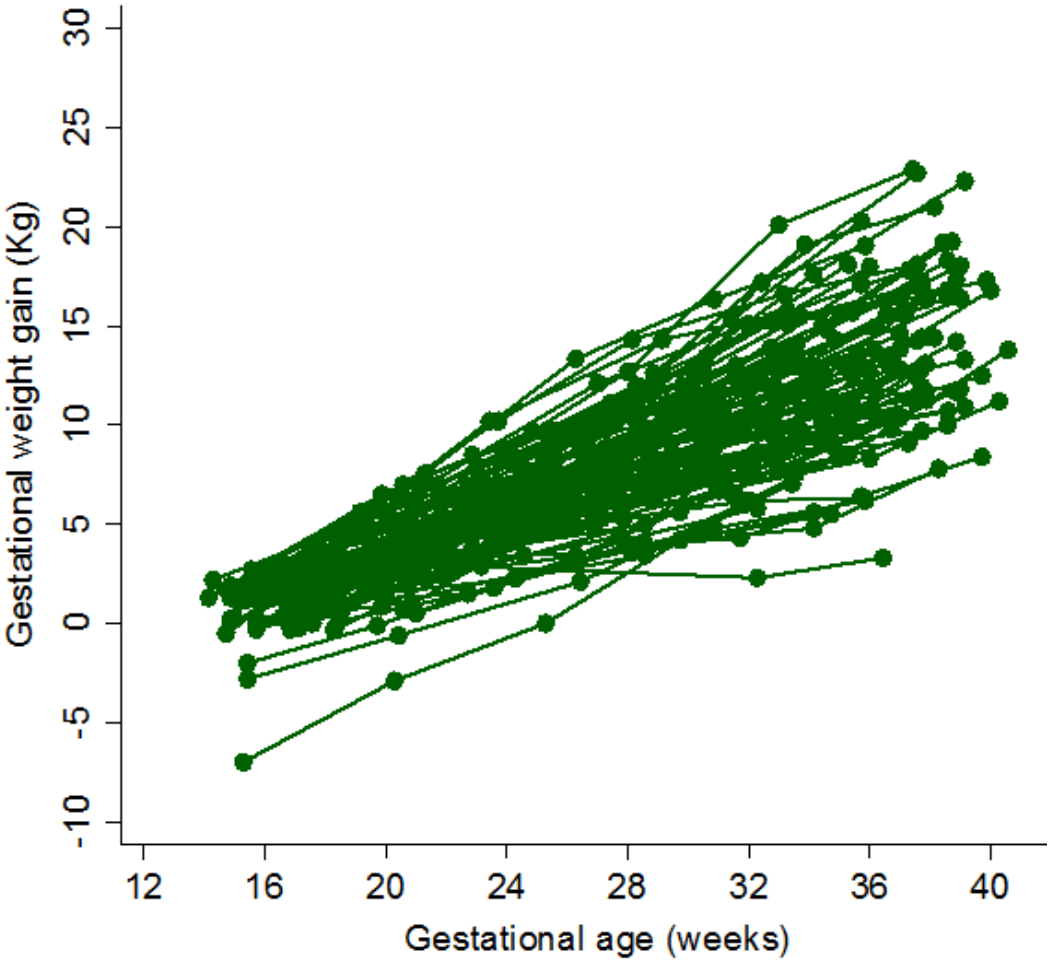
OVERVIEW


42+0
38+0
34+0
29+0
24+0
19+0
14+0
9+0
weeks
Follow-up visits
Weight only
Recruitment
Baseline information: height, weight and BMI

DATA COLLECTED



GWG trajectories of 100 randomly selected, normal-weight, healthy women with uncomplicated, live, singleton births

STATISTICAL CONSIDERATIONS

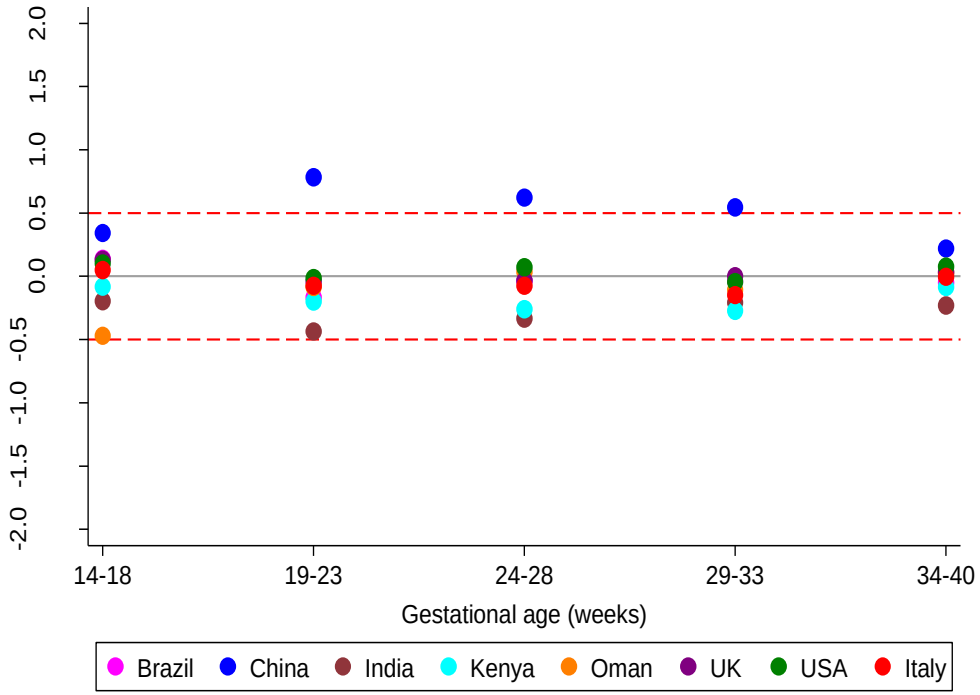
- Data collected from different sites → Can the data from the 8 sites be pooled together?
- Longitudinal data → What is the best method to construct the centiles?
- Lack of pre-pregnancy weight → How does a 1st trimester baseline weight affect the centiles?

DATA COMBINABILITY

Can we pool the data from the 8 geographically diverse participating centres to construct GWG charts?

3 approaches:

- Analysis of variance
- Sensitivity analysis
- Standardised site difference



Villar J et al. Lancet Diabetes Endocrinol 2014. / Altman DG and Ohuma EO BJOG 2012

CENTILES CONSTRUCTION

What is the best method available to construct centiles that takes in consideration the longitudinal nature of the data?

Multi-level, linear regression analysis adjusting for gestational age

Products:

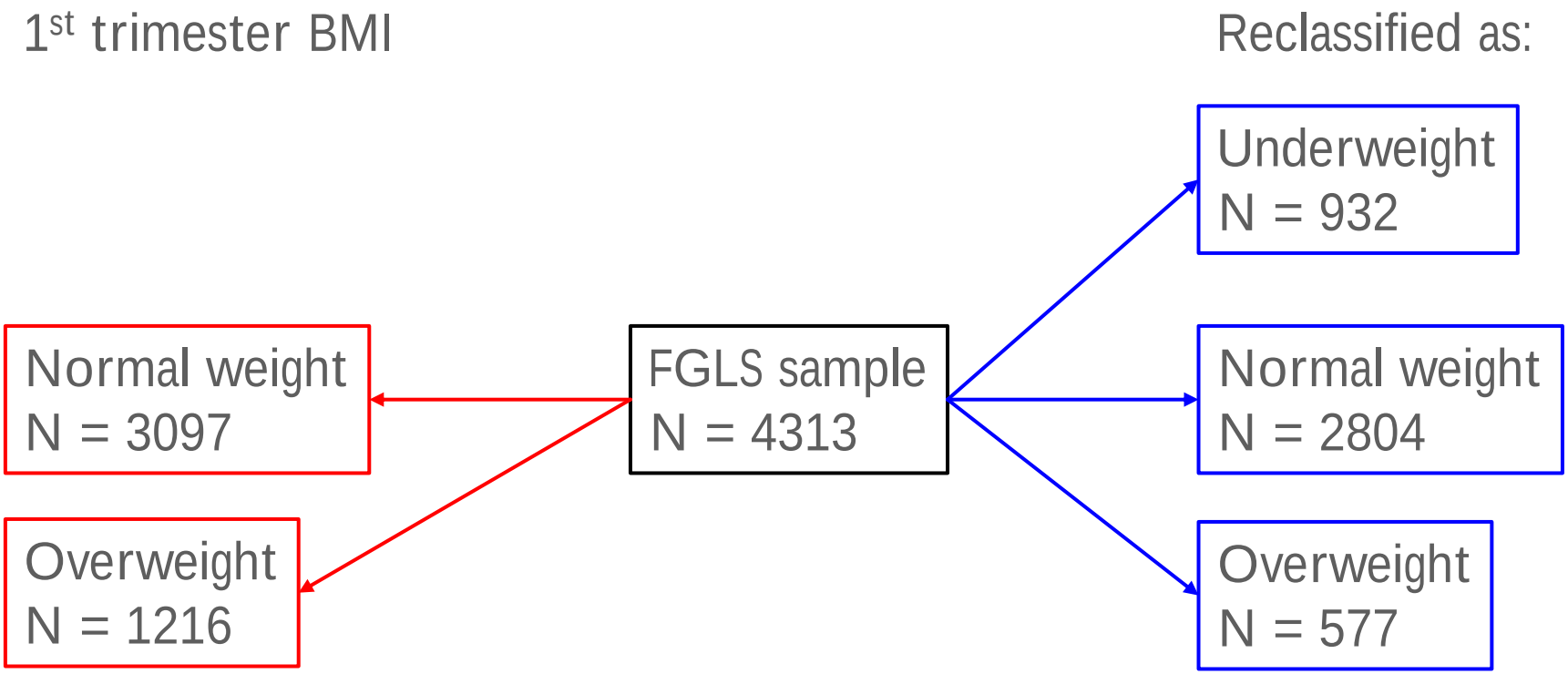
- Centile tables and graphs
- Centile equations

POSSIBLE BMI MISCLASSIFICATION?

Did 1st trimester BMI instead of pre-pregnancy BMI have an effect on our results?

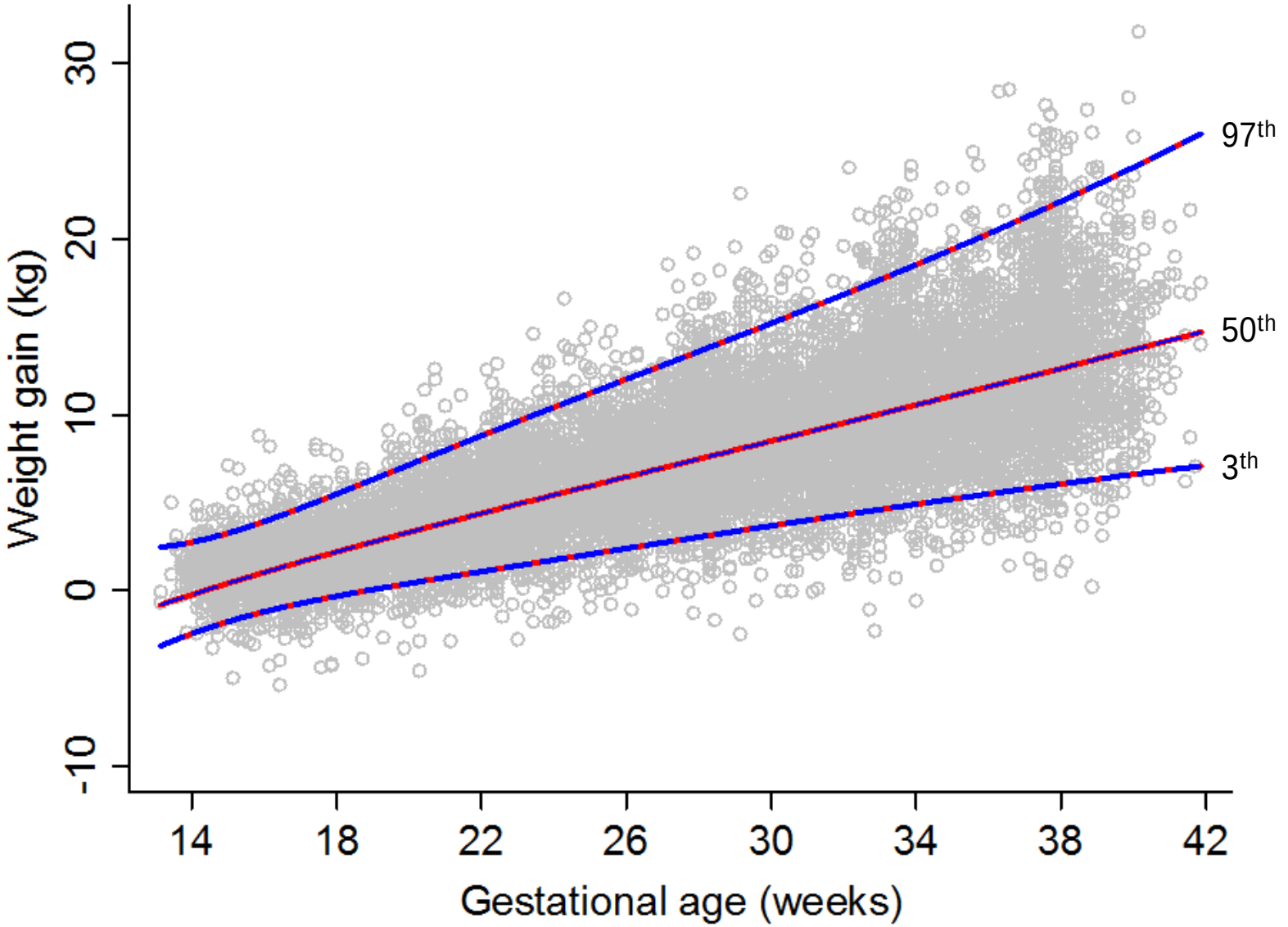
- Possible misclassification of women according to BMI as weight was obtained in the 1st trimester
- Reported GWG in 1st trimester: 0.5 - 2kg
- Analysis:
  - Reclassification of women who were within 2kg of the lower limit in the normal and overweight group
  - Repeat analysis with the reclassified BMI status and compare the 2 outcomes

RESULTS



WHO BMI classification (kg/m^2): BMI < 18.50 | BMI 18.5 – 24.99 | BMI 25.00 – 29.99 | BMI ≥ 30.00

GWG curves of women with a normal BMI based on 1st trimester weight (red) and reclassified as 'normal weight' (blue)



DATA SUMMARY

- 4,313 women → 24,977 measurements, out of which:
  - Normal-weight group, N = 3,097 → 14,809 measurements
- Number of measurements / woman, median = 6 (2 to 7)
- Median GA at 1st visit: 11.9 (1.4) weeks

BASELINE CHARACTERISTICS

	Normal BMI
	(N = 3097)
Maternal age (years)	28.2 (3.8)
Maternal height (cm)	162.3 (5.9)
Maternal weight (kg)	57.2 (6.5)
Paternal height (cm)	174.2 (7.3)
Body Mass Index (kg/m^2)	21.7 (1.8)
Gestational age at first visit (weeks)	11.9 (1.4)
Years of formal education (years)	15.1 (2.9)
Haemoglobin level <15 **weeks' gestation (g/dl)**	12.5 (1.1)
Married/cohabiting (%)	3020 (97.3)
Nulliparous (%)	2230 (71.8)

Mean (SD) or N (%)

PREGNANCY AND LABOUR COMPLICATIONS

	Normal BMI
	(N = 3097)
Pre-eclampsia (%)	12 (0.4)
Pyelonephritis (%)	9 (0.3)
Any sexually transmitted infection (%)	1 (0.0)
Spontaneous initiation of labour (%)	2127 (68.5)
PPROM (<37^{+0} **weeks' gestation) (%)**	46 (1.5)
Caesarean section (%)	1036 (33.4)
Preterm & spontaneous onset of labour (%)	82 (2.6)
Mother admitted to intensive care unit (%)	9 (0.3)

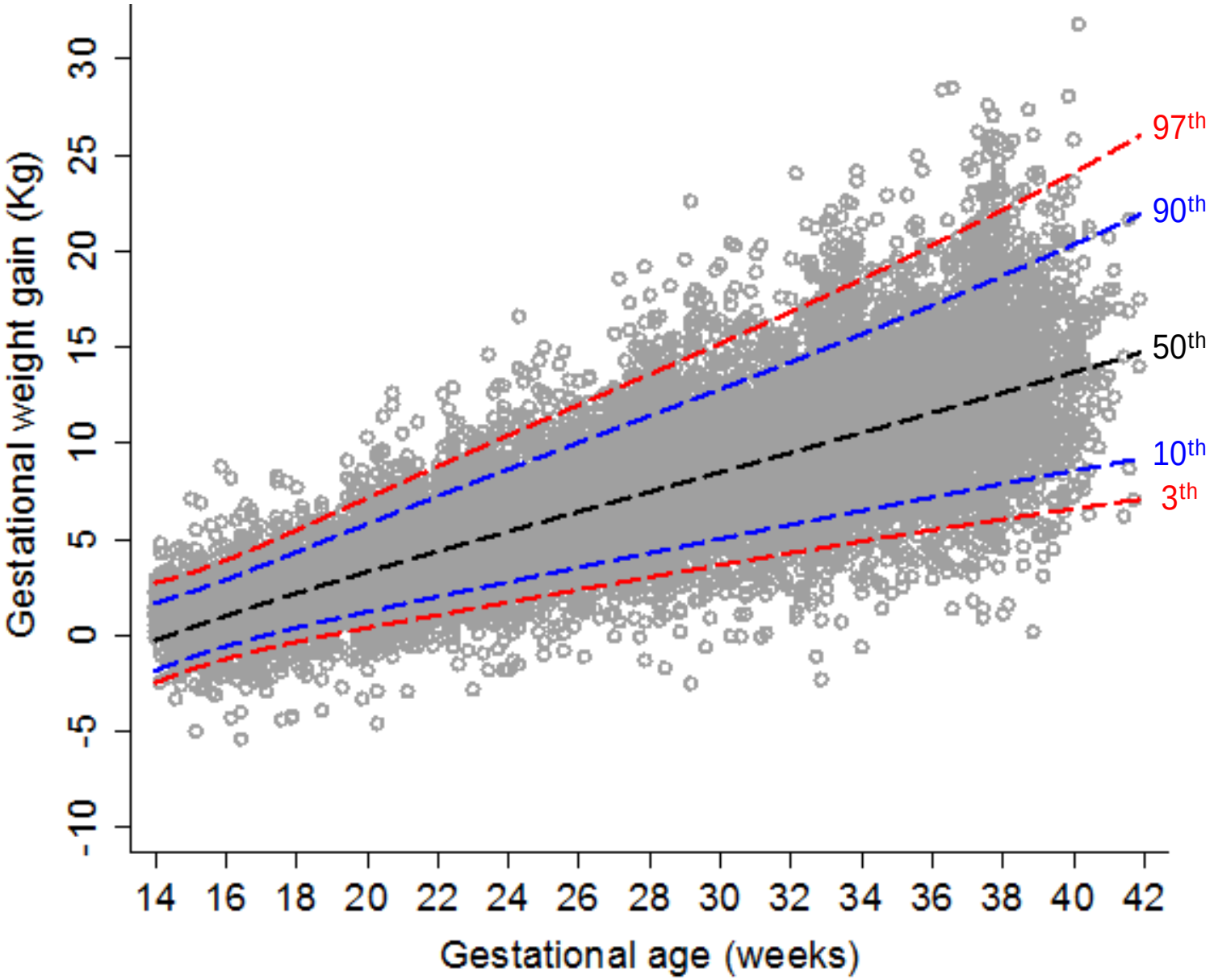
N (%)

NEONATAL OUTCOMES

	Normal BMI
	(N = 3097)
NICU admission >1 day (%)	160 (5.2)
Preterm (<37^{+0}) (%)	125 (4.0)
Term LBW (<2500g) (%)	99 (3.2)
Neonatal mortality (%)	4 (0.1)
Male sex (%)	1534 (49.4)
Exclusive breastfeeding at discharge (%)	2698 (86.9)
Birthweight (kg)	3.2 (0.4)
Birth length (cm)	49.3 (1.9)
Birth HC (cm)	33.8 (1.3)

Mean (SD) / N (%)

For normal-weight women



CENTILES CHARTS – NORMAL WEIGHT WOMEN

GA (weeks)	N	Centiles for GWG (kg)						
		3rd	10th	25th	50th	75th	90th	97th
15	473	-1.77	-1.14	-0.45	0.39	1.32	2.24	3.23
20	532	0.41	1.25	2.17	3.30	4.55	5.78	7.11
25	500	2.09	3.19	4.42	5.94	7.63	9.31	11.15
30	526	3.63	5.01	6.56	8.49	10.67	12.86	15.27
35	533	5.16	6.82	8.70	11.06	13.74	16.46	19.47
40	82	6.73	8.68	10.89	13.69	16.89	20.15	23.79

EQUATIONS TO CALCULATE CENTILES

Equations for estimating mean and standard deviation of normal-weight gestational weight gain according to exact gestational age (weeks).

Maternal measurements	Estimate	Regression equation
Normal weight **($18.5 \leq BMI \leq$** 24.9)	Median; log(GWG)	$1.382972 - 56.14743*GA^{-2} + 0.2787683*GA^{0.5}$
	SD; log(GWG)	$0.2501993731 + 142.4297879*GA^{-2} - 61.45345*GA^{-2}*LN(GA)$

SUMMARY

At term (40 weeks' gestation),

- On the 50th centiles, a normal-weight woman at booking has put on ~14.0kg (13.7kg)

HOW DO OUR RESULTS COMPARE TO?

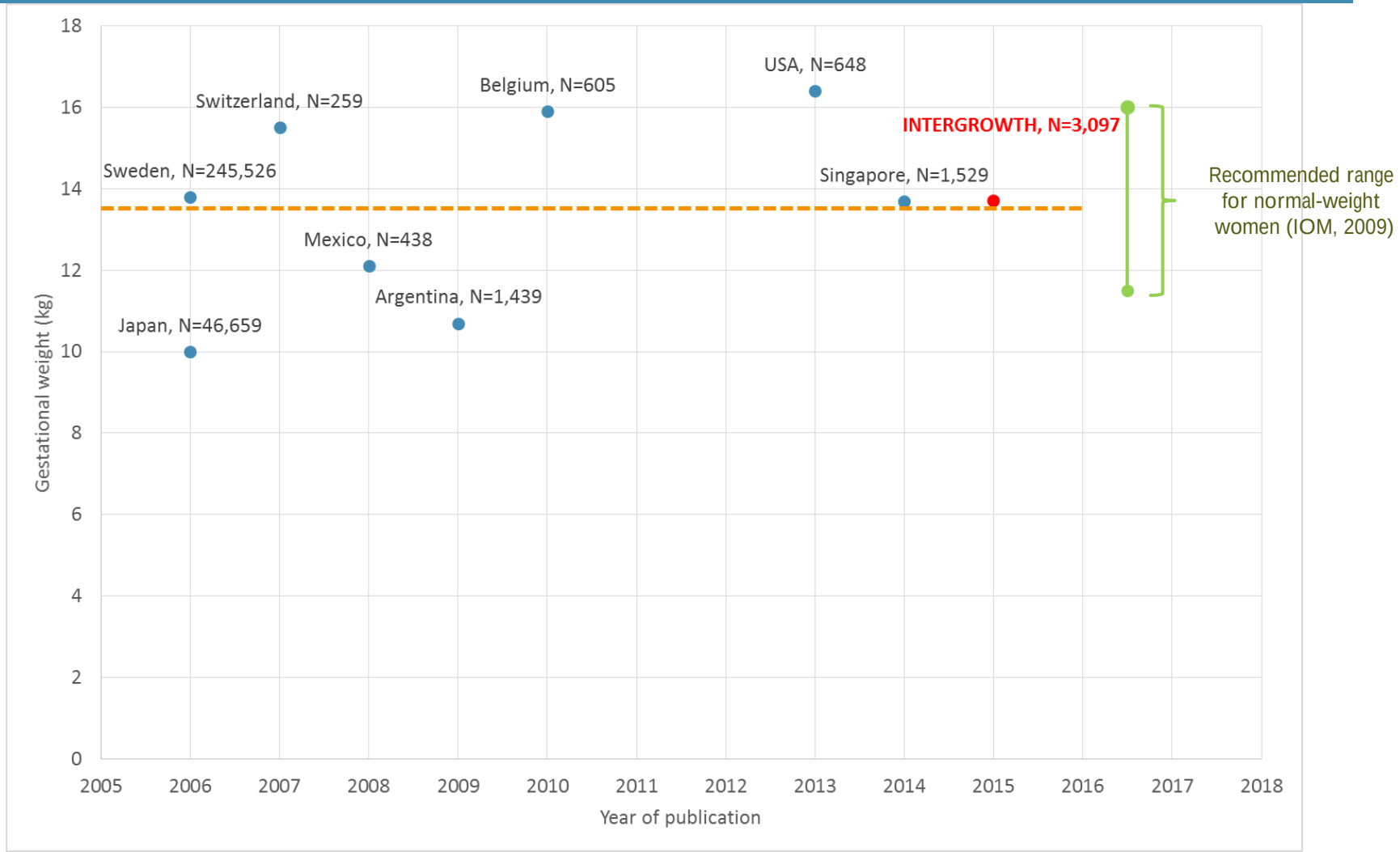
Single weight targets

- Healthy women in urban regions of Argentina: 10.7kg
- Low-risk urban population in Leuven, Belgium: 15.9kg
- Large cross-sectional studies of low-risk Japanese women: 10.0kg
- Healthy women in Mexico City: 12.1kg
- Multi-ethnic Singaporean population: 13.7kg
- Large cross-sectional studies of well-nourished in Sweden: 13.8kg
- Large cross-sectional studies of well-nourished women in Switzerland: 15.5kg
- Low-risk urban populations in Pittsburgh, USA: 16.4kg

Range targets

- IOM/NRC: 11.5 to 16.0kg for normal-weight women
- Healthy women in rural Malawi: 3.7-6.4kg

HOW DO OUR RESULTS COMPARE?



LIMITATIONS

- Use of 1st trimester weight as baseline:
  - Objective measurement better than recall
  - Practical as recruiting woman intending to conceive is difficult and might not be always appropriate
- No women classified as underweight (BMI <18.5kg/m^2) or obese (BMI ≥ 30.0kg/m^2)
  - Important as they are at-risk groups

CONCLUSION

- First multi-country study of GWG to:
  - Adopt a prescriptive approach
  - Employ highly trained anthropometrists to measure maternal weight (duplicate) prospectively
  - Use the same and standardised measurement equipment and protocols
- Produced GWG standards for healthy normal weight women

ACCOMPANYING PAPERS

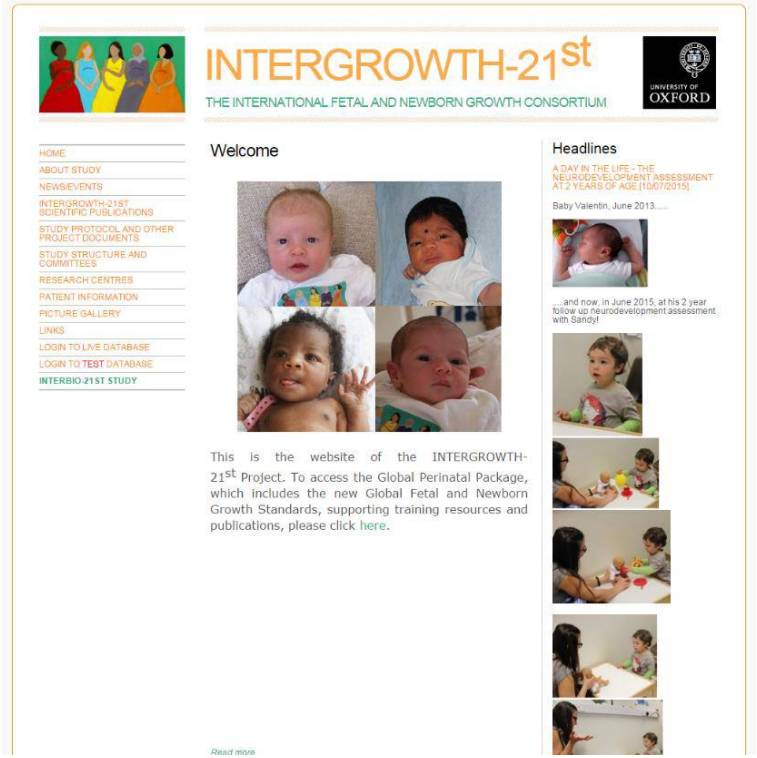
- Cheikh Ismail L, Bishop DC, Pang R, Ohuma EO, et al Gestational weight gain standards based on the women enrolled in the Fetal Growth Longitudinal Study of the INTERGROWTH-21st Project. 2016 (*BMJ Published*)

- Ohadike CO, Cheikh-Ismail L, Ohuma EO, et al. Systematic review of the methodological quality of studies aimed at creating gestational weight gain charts. 2015. *(Adv Nutr accepted)*

THANK YOU!

Visit our website:

http://www.intergrowth21.org.uk/



And the Global Health Network:

https://intergrowth21.tghn.org/

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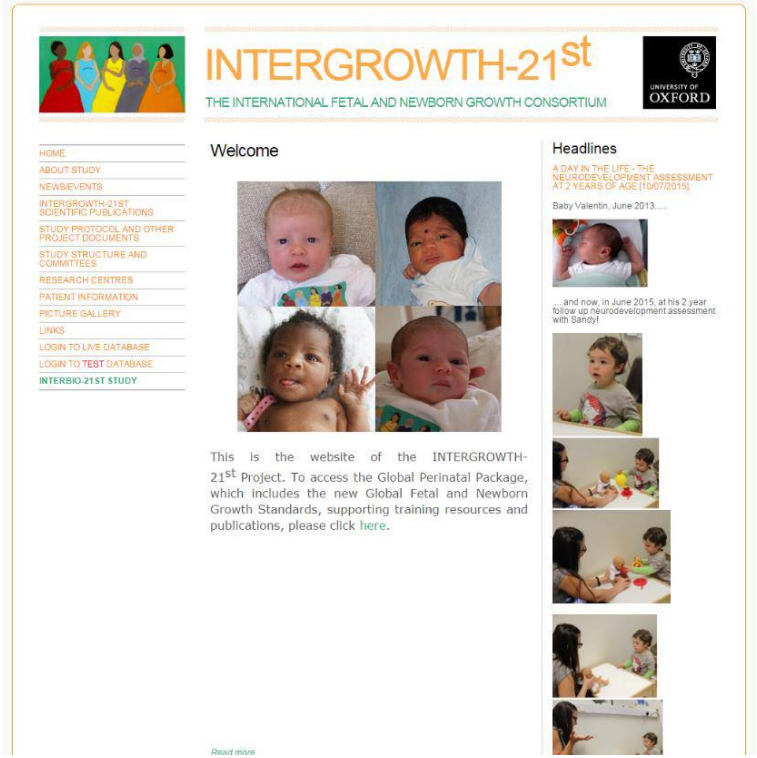

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