MATERNAL CONTRIBUTORS TO INTERGENERATIONAL NUTRITION, HEALTH, AND WELL-BEING:

Revisiting The Tanjungsari Cohort Study for Effective Policy and Action in Indonesia

DANONEINSTITUTE

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HEALTH, NUTRITION, AND WELLBEING OF INDONESIANS

Malnutrition, including stunting, remains one of the main challenges in Indonesian public health sector.

WHY TANJUNGSARI COHORT STUDY (TSC)?

Available data can be reanalyzed for evidence-based policy development.

THE IMPORTANCE OF IUGR FOR MALNUTRITION AND STUNTING RISK ASSESSMENT

IUGR predicts Low Birth Weight (LBW), growth retardation and mortality of infants.

MATERNAL & ENVIRONMENTAL DETERMINANT FOR GROWTH FALTERING IN THE FIRST 5 YEARS

Risk factors of shortness/stunting in under-five children (based on univariable binary logistic regression).

DETERMINANT OF SHORTNESS IN ADOLESCENT

Adolescent shortness in half of the cohort; Predictors of shortness in adolescent.

METABOLIC & COGNITIVE FUNCTION OF ADULTS WITH HISTORY OF LBW

Weight catch-up in the first 2 years may be a modulating factor for metabolic and cognitive performance.

LESSONS LEARNED

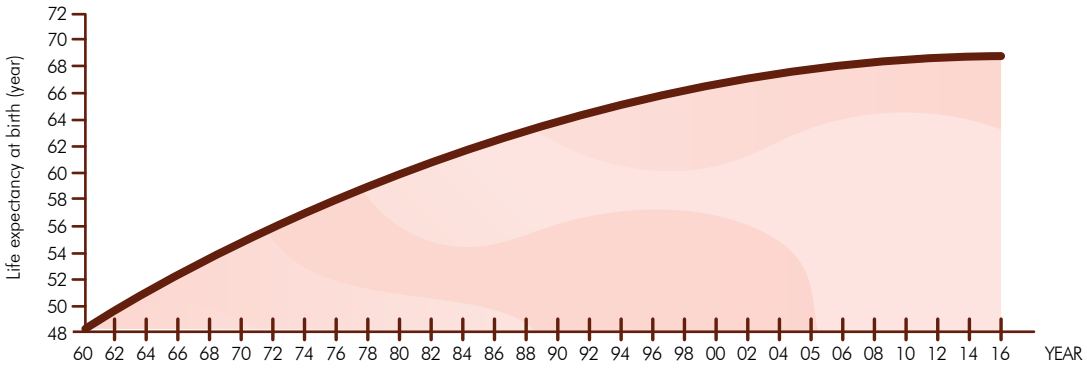
Pregnancy; infancy; adolescence; adulthood; social aspect.

RECOMMENDATIONS

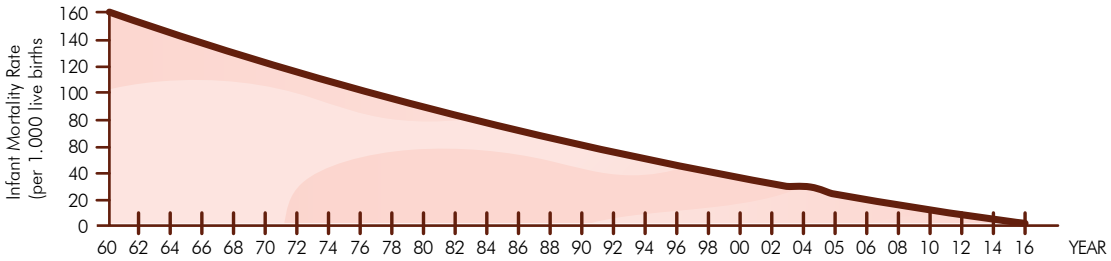
IUGR assessment; intervention for catch-up growth; nutritional adequacy through complementary feeding; education on exclusive breastfeeding & maternal nutrition; the role of women in community.

HEALTH, NUTRITION, AND WELLBEING OF INDONESIANS

- The advancement of health, nutrition, and well-being among Indonesians, while impressive over the period 1960-2017 for life expectancy and infant mortality remains variable across the nation and problematic overall.



A Indonesian life expectancy at birth (years) by year



B Indonesian infant mortality rate (per 1,000 live births) by year

	GDP (in constant 2010 USD)			
	1995 2,219.81	**2007** 2,750.62	**2013** 3,560.11	**2018** 4,130.66
Life expectancy at birth (years)	65.03	67.58	68.68	69.19 (2016)
IMR per 1,000 live births	50.4	30.9	24.5	21.4 (2017)
LBW (%)	10.3 (1997)	11.5	10.2	6.2
Underweight (%)	30.3	18.4	19.6	17.7
Wasting (%)	14.9 (1995)	13.6	12.1	10.2
Stunting (%)	48.1 (1995)	36.8	37.2	30.8

- Progress with nutritionally-related disease (NRD) has been claimed in the 2018 Baseline Health Research report (Riskesdas), with a further slight decline in infant mortality rate, prevalence of low birth weight, and underfive malnutrition. In contrast, there has been a significant increase in GDP during the same time frame as indicated in the above table. This shows **the nutritional issue has not received enough attention as much as the economic growth in Indonesia.**

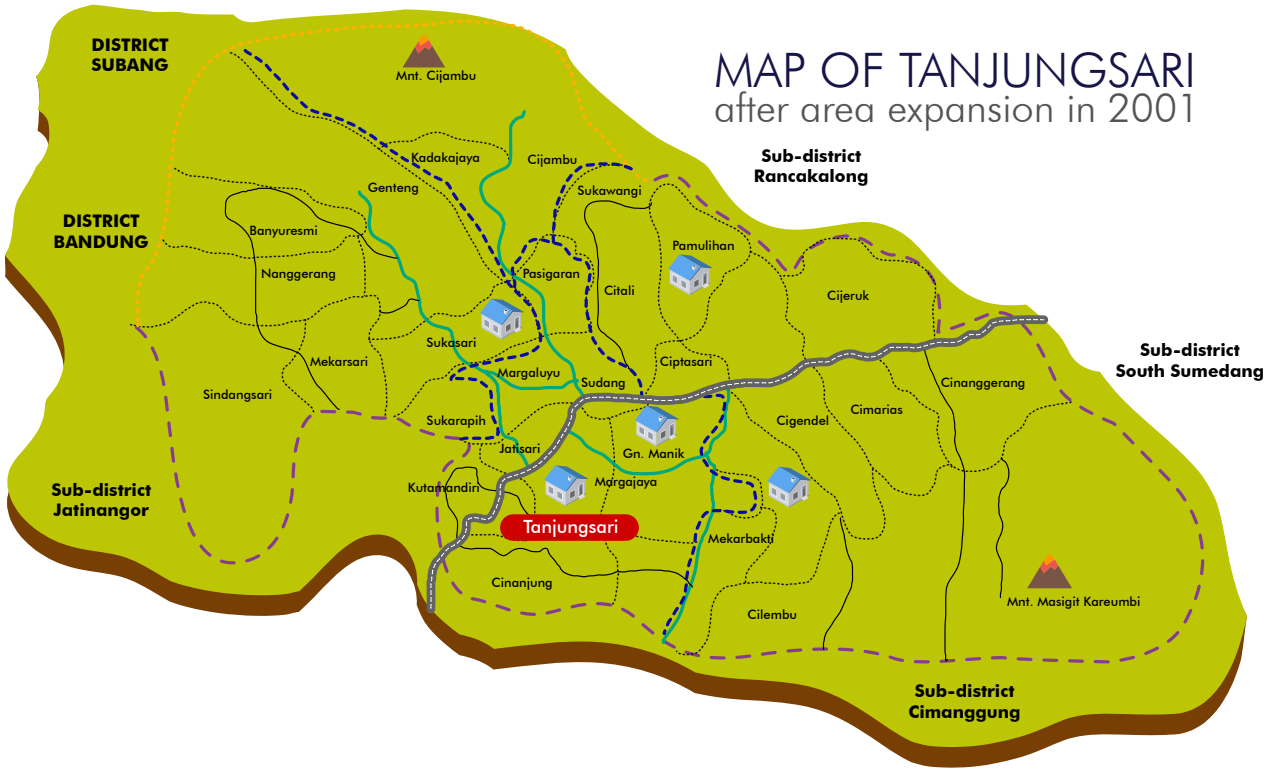
- **Malnutrition,** in any of its forms-underweight, wasting, and shortness or stunting (pathological shortness), and in any of the recognised at-risk populations-pregnant women, the newborn, and under-five children-**remains one of the main challenges for Indonesian public health sector that urgently need to be resolved.**

SECTION 1

WHY TANJUNGSARI COHORT STUDY?

TCS is a longitudinal study that started with the RAS (Risk Approach Strategy by Traditional Birth Attendants) research project in October 1987-December 1989.

A birth cohort was established in 1988–1990 in the Tanjungsari subdistrict (West Java, Indonesia). It intended to design and implement evidence-based policy to reduce pathological shortness (stunting) in under-five children in Indonesia.



SECTION 1

WHY TANJUNGSARI COHORT STUDY?

TCS focuses on the factors that affect the growth and development of under-five and young children, including later life, cognitive function, and metabolic profile.

Cohort observation for 21 years (1988-2009) thus covering three generations (from grandmother to grandchildren). Additionally, further observation on later life was extended until 2017.

HISTORY OF THE SAMPLE SIZE OF TANJUNGSARI COHORT STUDY:

Jan 1988 - Dec 1989
4,440 pregnant women (G1)
4,108 singleton births (G2)

continued recruitment

March 1990
additional 590 singletons
Total: 4,698 singleton births (G2)

3,890 children with data for 2-month follow-up

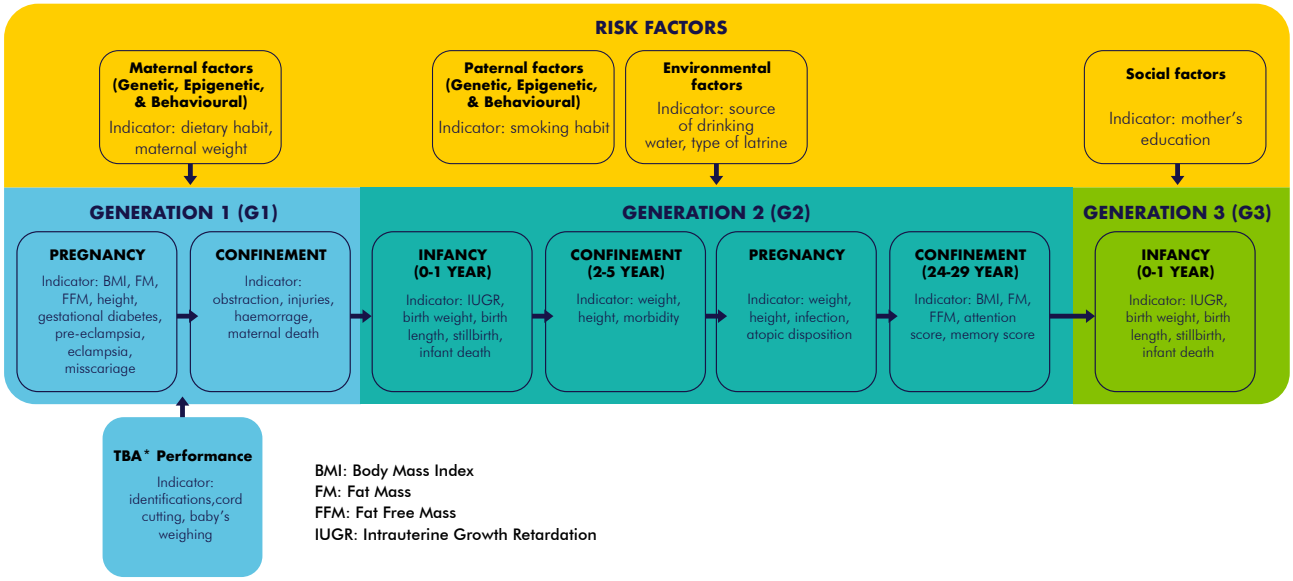
1991-1992
3,144 children two years old

1994-1995
3,795 children with data for 5-years follow up

2001-2002
3,148 12 years old children

2009-2012
(Fetal Origins of Adult Disease or FOAD Studies)
Samples from 3,548 adult (G2)

Conceptual Framework for the intra- and inter-generational TCS of maternal and child health with example indicators



BMI: Body Mass Index
FM: Fat Mass
FFM: Fat Free Mass
IUGR: Intrauterine Growth Retardation

- The Tanjungsari Cohort Study merits revisitation for at least 3 reasons: (1) Observation of 3 generations since 1988; (2) re-analysis for potential links between ecological factors and nutritionally-related health (NDR) outcomes; (3) Valuable insights into public health and nutritional policy across the lifespan may be provided.

SECTION 2

THE IMPORTANCE OF INTRAUTERINE GROWTH RETARDATION (IUGR) FOR MALNUTRITION AND STUNTING RISK ASSESSMENT

WHY IUGR?

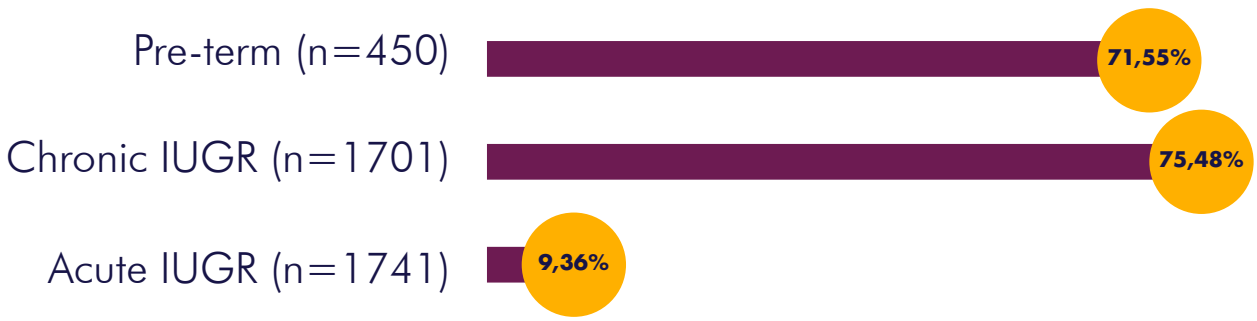
An important indicator
for child growth and development, intellectual potential, as well as its sequences in later life.

IUGR might contribute to the development of non-communicable disorders in adult life
(e.g. obesity, type 2 diabetes, hypertension, heart disease, etc.)

It leads to the development of less potent cellular immunity
thus higher risk of severe infectious disease in children.

IUGR Percentage in Tanjungsari Cohort Study
(Alisjahbana et al., 2019)

Chronic IUGR, Acute IUGR, and Pre-term based on Body Weight and Body Lenght
(Alisjahbana et al., 2019)



SECTION 2

THE IMPORTANCE OF INTRAUTERINE GROWTH RETARDATION (IUGR)
FOR MALNUTRITION AND STUNTING RISK ASSESSMENT

Due to the large variation in weight and length at particular gestational age, Alisjahbana et al. developed another means of classifying infants as non-IUGR or IUGR using only BW and BL.
Newborns are considered to have impaired fetal growth (IUGR) in two circumstances:

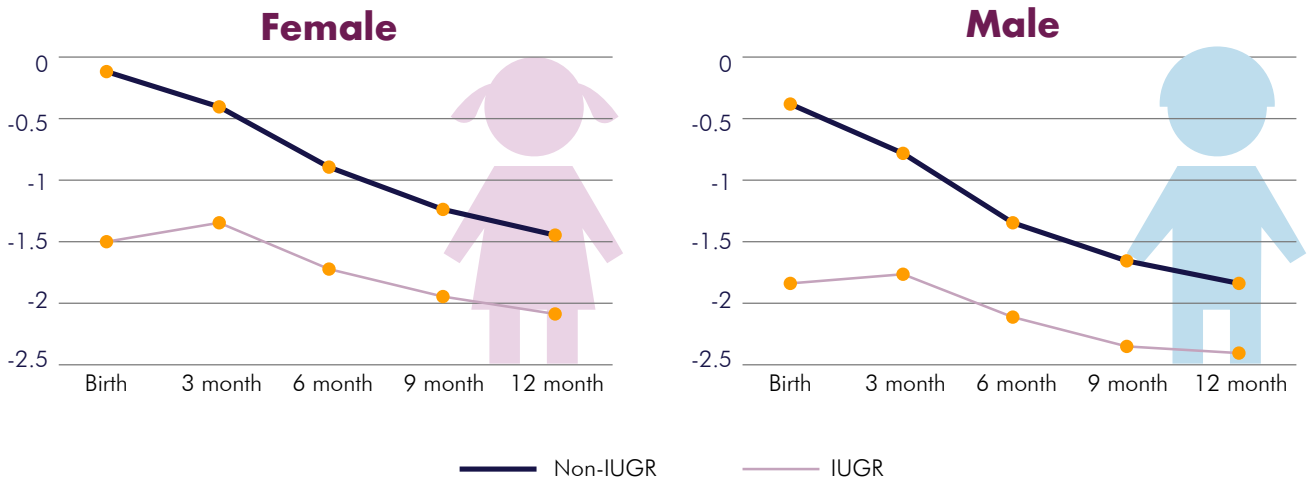
1. A combination of BW <2700 g with a normal BL of ≥ 48 cm was considered to imply acute IUGR.
2. A combination of BW <3000 g and BL < 48 cm implies chronic IUGR.

IUGR based on BW and BL identifies a larger group of at-risk infants. Including BL as a determinant factor has contributed in optimizing nutritional status in the first 1,000 days of life.

IUGR is different from Pre-term!

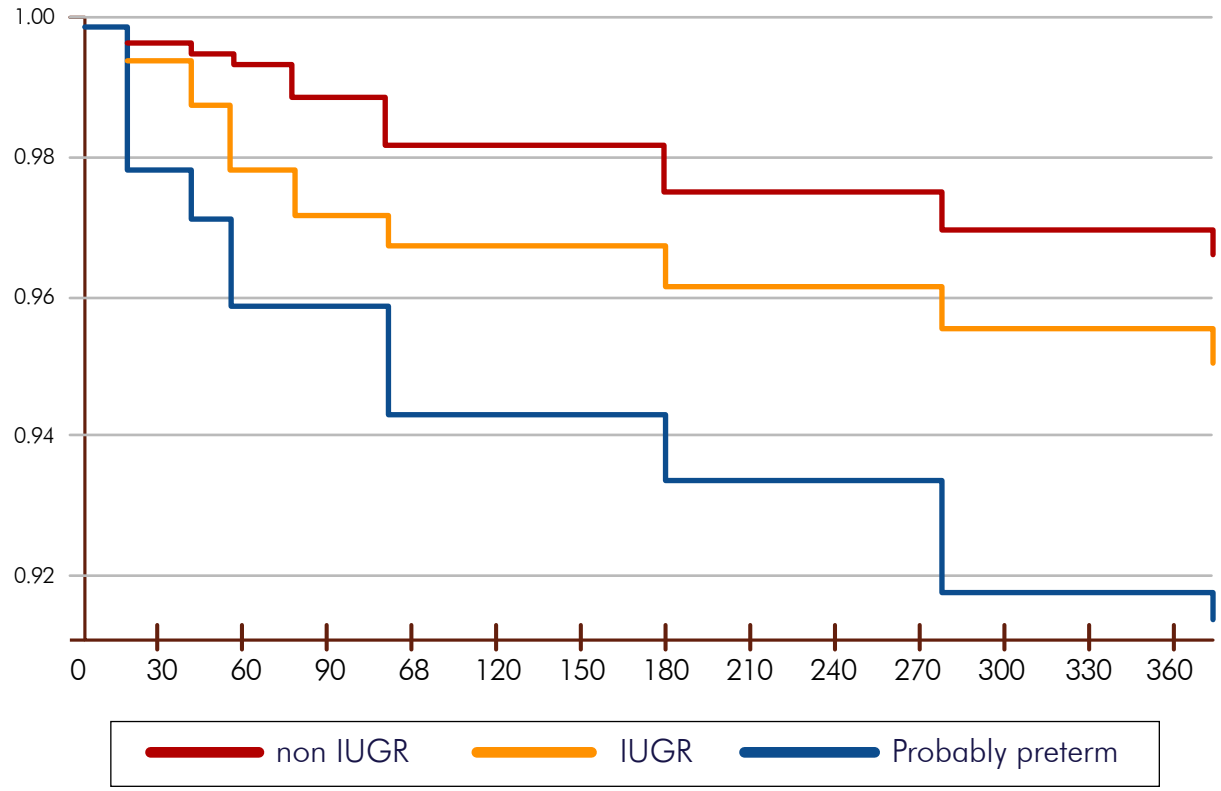
- IUGR: A condition in which an unborn baby is smaller than it should be as it is not growing at a normal rate inside the womb.
- Pre-term: Birth occurring earlier than 37 weeks gestational age.

Comparation between the growth of IUGR and non-IUGR infants (based on mean WAZ and HAZ in the first year) (Source: Alisjahbana et al., 2019)
The growth curves for the IUGR infants were consistently below those of the non-IUGR infants, both in females and males. After 3 months, the growth in both groups began to progressively falter until the age of 12 months. In the Non-IUGR and IUGR groups, the HAZ was different between genders. In fact, the mean HAZ deviated by a larger extent than did the WAZ. Below are the figures for HAZ in infancy for both female and male in the non-IUGR and IUGR groups.



HAZ in infancy for female and male in the non-IUGR (n=691; 886) and IUGR (n=754; 693)

Infant mortality based on IUGR



Kaplan-Meier survival curve of infants in the first year of life by IUGR category.

Throughout infancy, the survival curve on non-IUGR infants was better than the IUGR infants, whereas preterm infants (which can also include infants with birth weights of 2,500-2,700 g) had the highest probability of death.

Within the IUGR and preterm categories, significant differences in the survival curve were identified:

1. At 3 months of age, the risk of death for the LBW babies was 3.1x higher than the normal birth weight (≥2,500 g) babies.
2. At 3 months of age, the risk of death for the preterm babies were 2.9x higher than the non-IUGR babies.
3. The risk for IUGR babies was 1.7 higher than the non-IUGR babies.

The Hazard Ratio of Risk Factors for Infant Mortality
(Source: Alisjahbana et al., 2019)

The risk of IUGR and other determinants of infant mortality are calculated using hazard ratio and/or adjusted hazard ratio (aHR). Among the most significant factors are **IUGR, sex, education, and latrine.** Maternal education of less than 6 years and latrine usage type are significantly associated with mortality in the crude HRs, but not when adjusted for sex and IUGR.

44% **Latrine**
Unimproved latrine condition increases the risk of infant mortality by 44%

51% **Maternal Education**
Maternal education less than 6 years increases the risk of infant mortality by 51 %

60% **IUGR**
The IUGR infant is at risk of death by 60%

70% **Sex**
A male infant is at risk of death by 70%

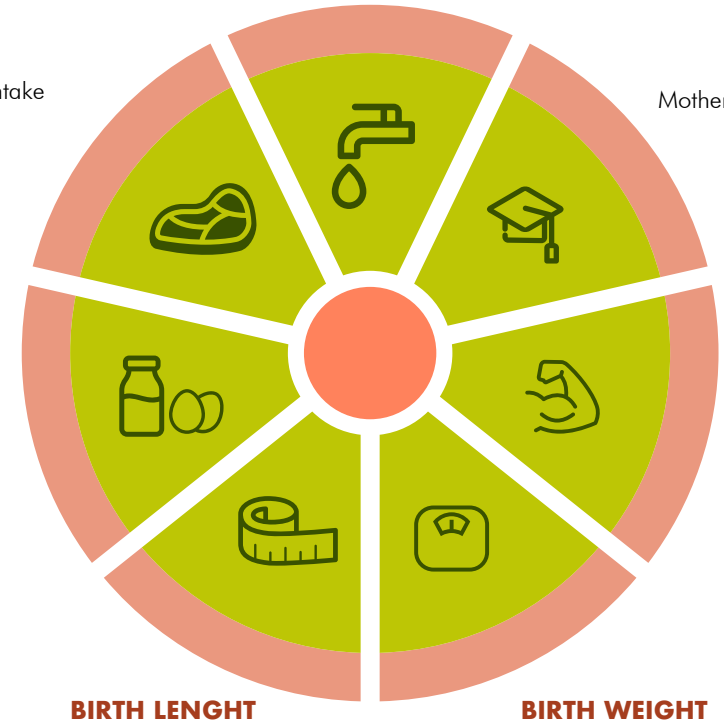
SECTION 3

MATERNAL & ENVIRONMENTAL DETERMINANT FOR GROWTH FALTERING IN THE FIRST 5 YEARS

Risk factors of shortness/stunting in under-five children based on univariable binary logistic regression
(Sofiatin et al, 2019)

WATER
Unimproved source of drinking water
= 1,5x risk of shortness/stunting.

PROTEIN INTAKE (6-24 MONTHS)
No additional protein intake 6-24 months (MP-ASI)
= 1,45x risk of shortness/stunting.



EDUCATION
Mother formal education ,6 years
= 1,25x risk of shortness/stunting.

PROTEIN INTAKE (0-6 MONTHS)
No additional protein intake 0-6 months
= 1,3x risk of shortness/stunting.

MUAC
MUAC of Mother
= 1,43x risk of shortness/stunting.

BIRTH LENGHT
Short Birth Weight
= 2,43x risk of shortness/stunting.

BIRTH WEIGHT
Low Birth Weight
= 2,38x risk shortness/stunting.

SECTION 4

DETERMINANT OF SHORTNESS IN ADOLESCENT

The 12-year tracking of maternal-child dyads in the rural Tanjungsari in Indonesia reveals that a combination of intrauterine, maternal education, environmental and interval growth performance factors are associated with severe shortness or stunting in early adolescence at age 12 (Sasongko et al., 2019).

Adolescent shortness was found in almost half of the cohort followed from birth. It was associated, among others, with birth weight as well as several individual, maternal and environmental factors evident at age 2, along with atopic disposition at age 12. Nevertheless, stature itself may not constitute a health risk over and above the associated socio-environmental conditions.
Shortness is not necessarily a nutritional problem and may represent nutritional adaptation.

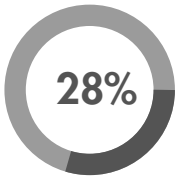
SECTION 4

DETERMINANT OF SHORTNESS IN ADOLESCENT

Bivariate and Multivariate analysis of predictors of shortness in adolescent (12 years old):

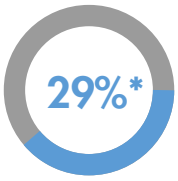
Complementary Feeding

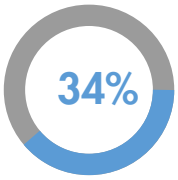
Consumption of complementary feeding in the form of milk at age 2 years reduced the risk of stunting by 22%, indicating the importance of nutritional adequacy.



Infectious Disease Risk

History of infectious disease at age 12 years increased the risk of shortness by 28%.



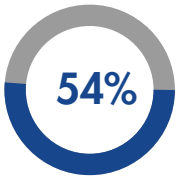


Atopic Disease Risk

History of atopic disease at age 12 years increased the risk of shortness by 34% or 29%*.

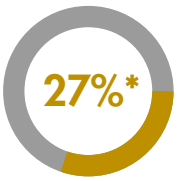
Low Birth Weight

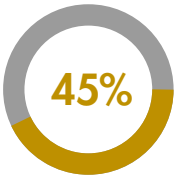
History of Low Birth Weight increased the risk of shortness by 61% or 64%*.



Shortness at Age 2

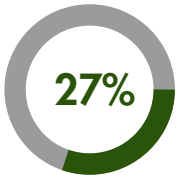
Shortness at age 2 increased the risk of shortness in adolescent by 54%.





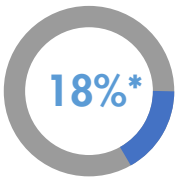
Drinking Water

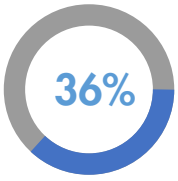
Unimproved source of drinking water increased the risk of shortness in adolescent for 45% or 27%*.



Maternal Literacy

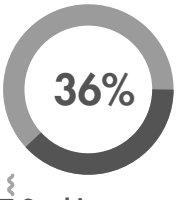
Mothers who were illiterate / had <6 schooling years increased the chance of having stunted children by 27% or 19%*.





Latrine

Unimproved latrine increased the risk of shortness in adolescent by 36% or 18%*.



Smoking Exposure

Exposure to smoke increased the risk of shortness in adolescent by 36%.

Breastfeeding

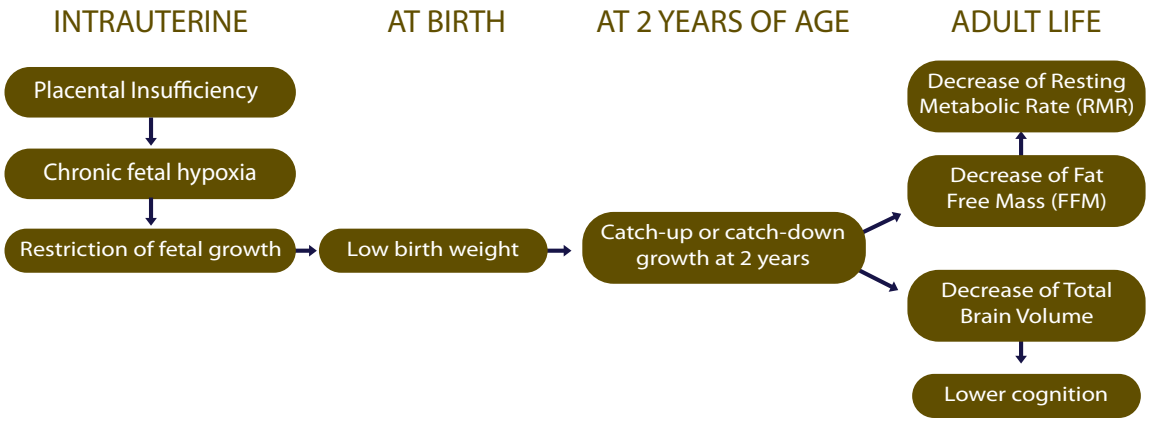
Stop breastfeeding at age 2 years might decrease the risk of shortness in adolescent by 19%.

Note: *Percentage based on multivariate analysis.

SECTION 5

METABOLIC & COGNITIVE FUNCTION OF ADULTS WITH HISTORY OF LBW

TSC Conceptual Framework for birth weight, growth at 2 years, resting metabolic rate (RMR) and cognition:



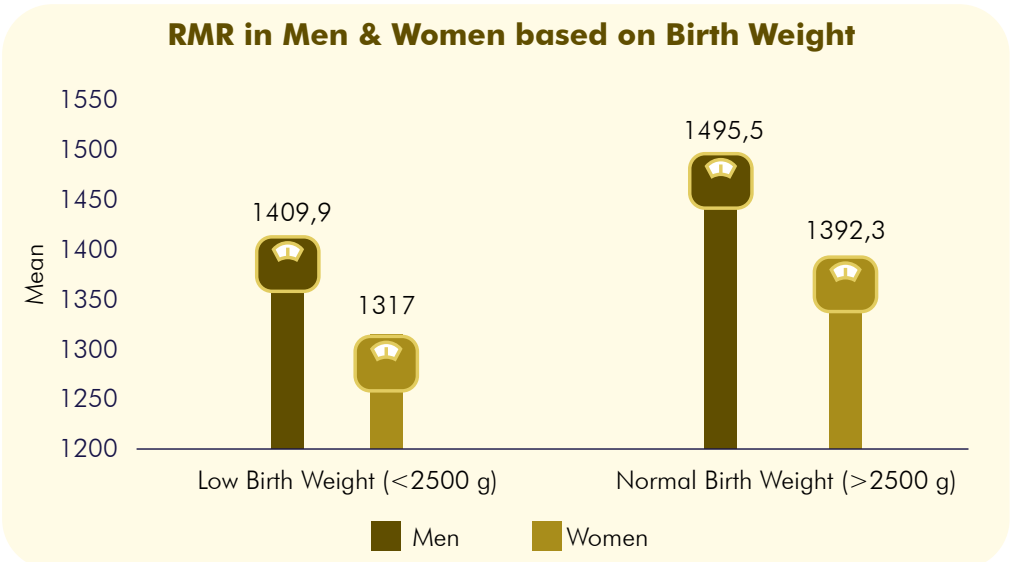
RMR is positively associated with birth weight, body weight at 2 years age, body mass index, and fat-free mass in adult life (Nugraha et al., 2019).

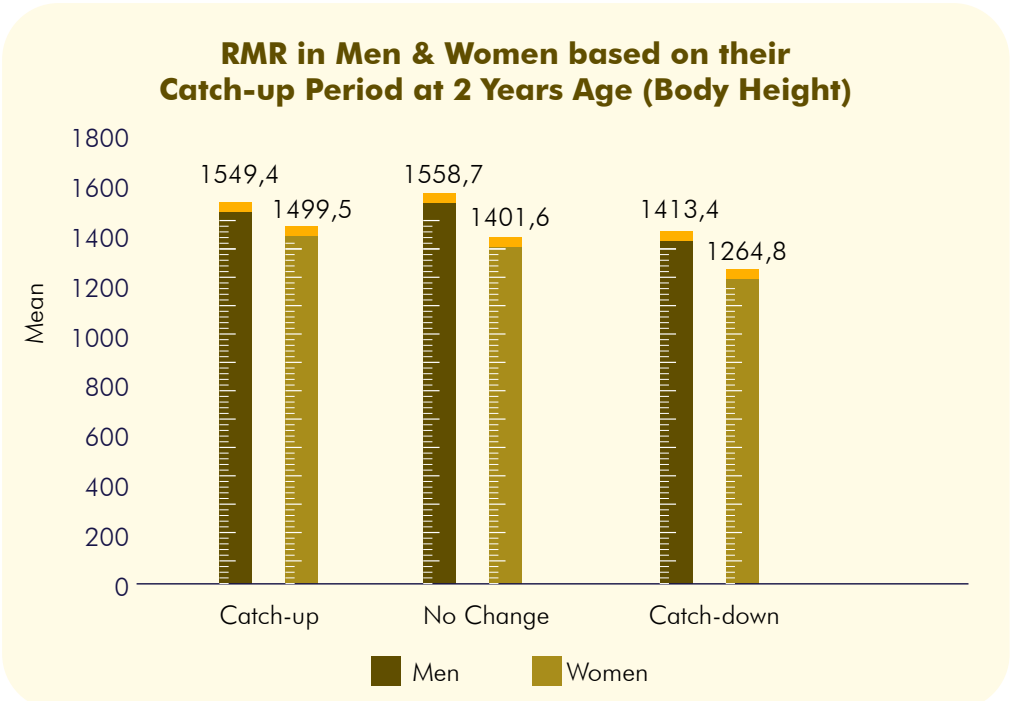
How the RMR was measured?

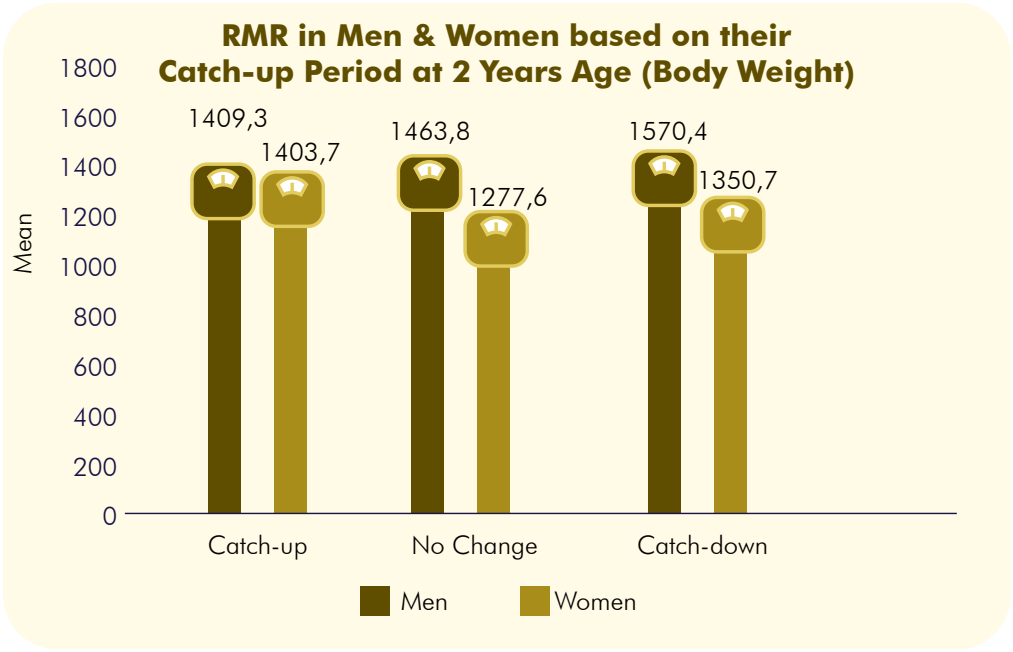
RMR was measured using indirect calorimetry (QUARK RMR, Cosmed, Rome, Italy). Measurements were recorded at 5-s intervals for 16 minutes. Calibration was performed prior to every examination. Oxygen consumption (VO2) and the production of carbon dioxide (VCO2) in litres per minute, as well as the tidal volume, were measured. RMR values were obtained in kilocalories (kcal) per day by using the Weir Formula: [3.941 (VO2) + 1.106 (VCO2)] x 1440.

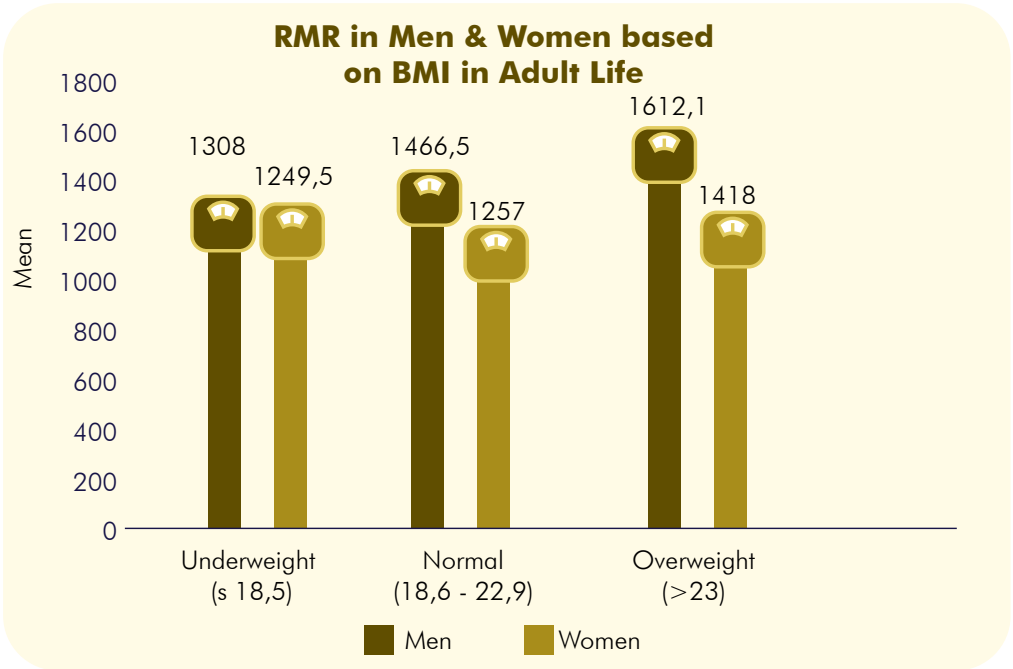
MR (kcal/24 h) in men and women according to birth weight, catch-up at 2 years, and BMI in adult life

(Nugraha et al., 2019)





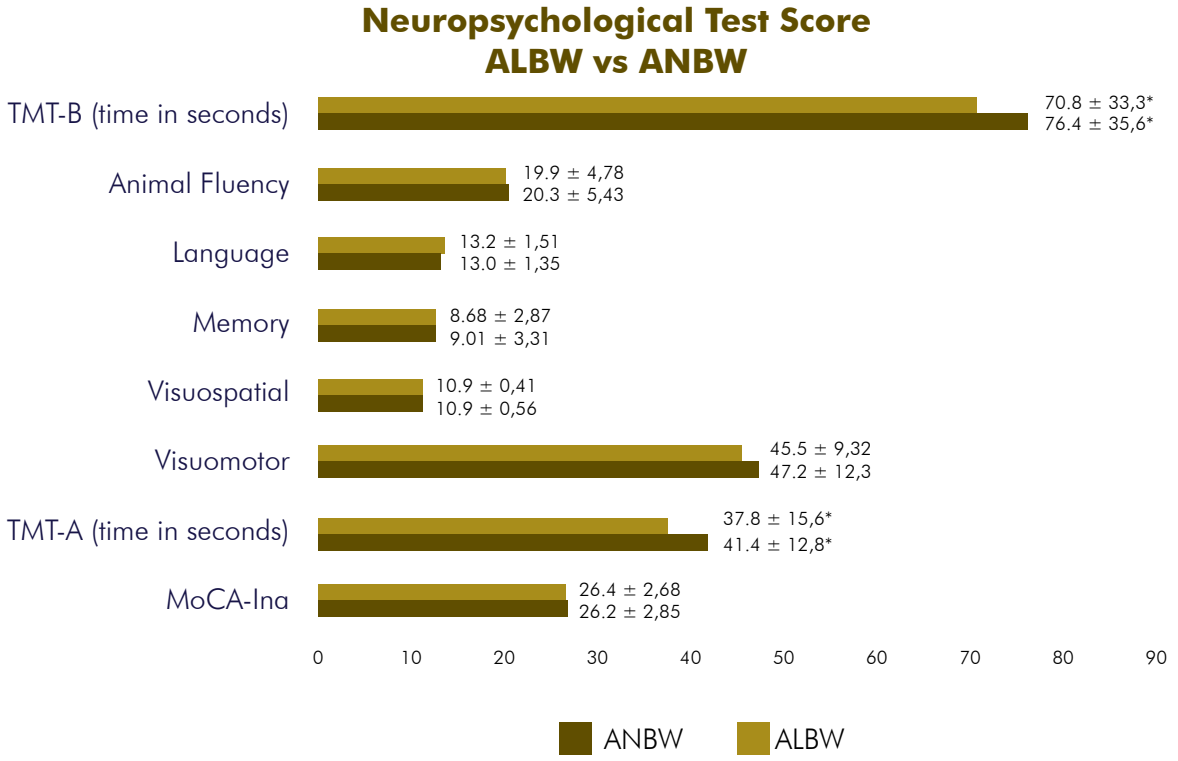




Based on the statistic above, no significant difference was discovered in the RMR between birth weight groups among the men or women. At 2 years age height was associated with RMR; in adulthood, BMI was associated with RMR.

Body size (weight and height/length) at 2 years of age is a crucial factor in determining RMR during adulthood. Therefore, improving nutritional status that affects body size (catch-up) may independently affect RMR in adulthood regardless of birth weight.

Comparison of neuropsychological test scores between Adulth with history of Low Birth Weight (ALBW) and Adulth with history of Normal Birth Weight (ANBW) groups (Nugraha et al., 2019)



In this study, ALBW participants have the same level of education, employment, monthly income, and marital status compare to ANBW participants. It is supposed that all ALBW participants might have a much milder cognitive deficit and managed to catch-up in education and social-economic attainment in adult life.

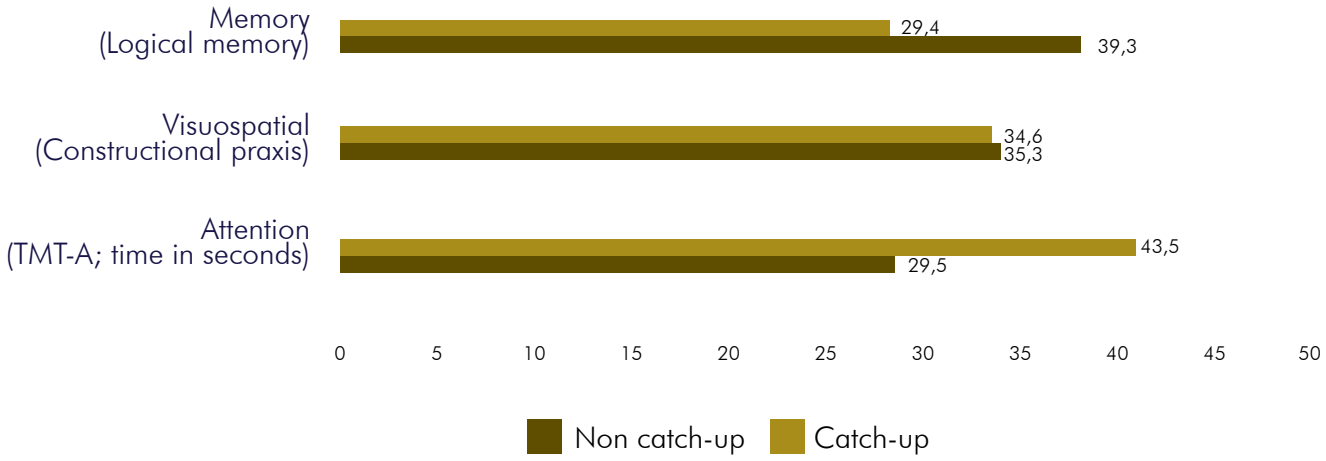
Even though ALBW participants have the same achievement for educational level, socioeconomic attainment, and the global cognitive screening test compared to ANBW participants, ALBW participants still have lower scores for specific cognitive domain tests of attention compared to those with ANBW. This subtle cognitive deficits in attention (TMT-A) are significant in adult life (41,4 ± 12,8 vs 37,8 ± 15,6). It takes a much longer time for ALBW participants to finish the test compared to those of ANBW groups.

***TMT-A and TMT-B are valued based on time per second. The faster the processing time, the better the test result.**

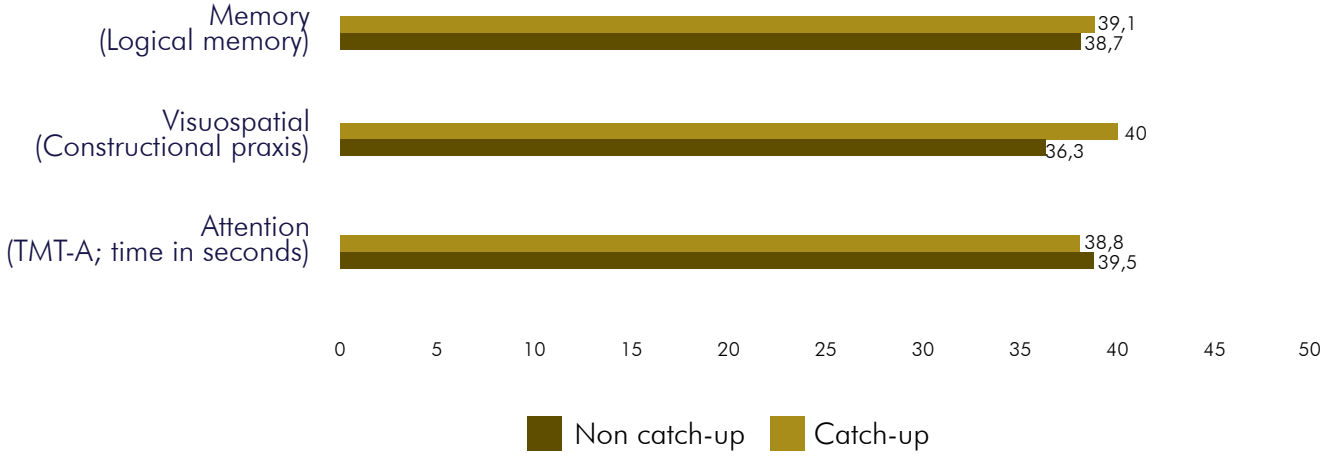
Comparison of neuropsychological test scores between catch-up and non-catch-up subjects

(Nugraha et al., 2019)

Neurophysical Test Score Comparison between Catch-up & Non Catch-up in ALBW Group



Neurophysical Test Score Comparison between Catch-up & Non Catch-up in ANBW Group



The catch-up period has a role in influencing cognitive achievement such as memory, visuospatial, and attention. In the ALBW group, catch-up is associated with superior attention and memory function compared with their counterparts who do not experience catch-up growth. This is reflected in the shorter time catch-up subjects take to finish the TMT-A test and by the higher score that the catch-up participants obtained on the logical memory test. By contrast, the catch-up subjects in the ANBW group show poorer visuospatial function, as reflected by their lower score on the constructional praxis test. These findings indicated that weight catch-up may be a modulating factor for birth weight and cognitive achievement.

SECTION 6

LESSONS LEARNED

PREGNANCY

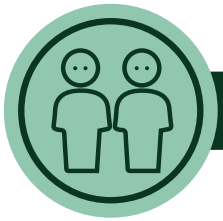
- IUGR classification based on a combination of body weight and body length identified a larger group of infants at health risk compared with Low Birth Weight. **Only 23.6% of infant mortality may be avoided if health programmes concentrate solely on infants with Low Birth Weight; while targeting interventions to preterm and IUGR newborns could potentially prevent more than 60.2% of infant death.**

INFANCY

- **Growth-retarded infant never reaches their growth potential** and remain smaller and lighter than their peers.
- **The first week, first month and first 90 days after birth** were the most vulnerable age periods regarding infant mortality.
- Low Birth Weight is a risk factor for shortness/stunting. **Adding complementary protein at 6-24 months may prevent shortness/stunting.**

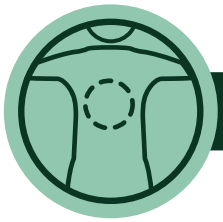
SECTION 6

LESSONS LEARNED



ADOLESCENCE

- Shortness/stunting in adolescents presumably reflects the **cumulative effects of poor nutrition, infection and environmental factors** operative from the fetal period through young adulthood.
- More attention should be paid to adolescent girls who are short/stunted because of the **possible adverse consequences in the event of pregnancy,** where intergenerational nutritional disorders may occur.
- **Shortness/stunting at age 2 years is a risk factor for shortness/stunting in adolescence.** Children who were stunted at 2 years are more likely to remain stunted and not recover.



ADULTHOOD

- Adult with history of low birth weight has a poorer **attention span** compared to adult with history of normal birth weight.
- **Clinical characteristics associated with RMR:** birth weight, weight at 2 years of age, BMI, and fat-free mass in adult life.
- Weight gain and catch up are associated with superior memory performance in adults with history of low birth weight. However, even though the TCS study indicates that there are cognitive benefits with weight catch-up at 2 years of age, caution should be taken in interpreting this because **catch-up may also increase vascular risk factors** such as high levels of sugar in blood (hyperglycemia) and increased waist circumference, as well as Body Mass Index.

SOCIAL ASPECT

- The habit of prioritizing men during the meal is still practiced in rural areas, thus affecting the quality of the mother's nutritional intake. Therefore, the **promotion of exclusive breastfeeding should be complemented by educating the family on the importance of maternal nutrition.**
- Female community health volunteer is the key to strengthen the healthcare system in rural settings, especially with regards to mother and child's nutrition.

SECTION 7

RECOMMENDATIONS

1. IUGR assessment at the Puskesmas level should be conducted.
2. Strengthening intervention during Window Opportunity for Catch-Up Growth at different ages.
3. More attention should be addressed to under-five children with history of Low Birth Weight, especially nutritional adequacy through consumption of, amongst others, complementary feeding in milk form aiming to reduce the risk of shortness/stunting.
4. The promotion of exclusive breastfeeding should be accompanied by educating the family on the importance of good maternal nutritional status.
5. Continuous support should be given to the education of women and the role of women in community development as it pertains to child growth and development.

GLOSSARY

- ALBW: Adult with history of Low Birth Weight
- ANBW: Adult with history of Normal Birth Weight
- BMI: Body Mass Index
- FFM: Fat Free Mass
- HAZ: Height for Age Z-score
- IMR: Infant Mortality Rate (per 1,000 lives births)
- IUGR: Intrauterine Growth Retardation
- MoCa-Ina: Indonesian version of Montreal Cognitive Assessment
- MUAC: Middle-Upper Arm Circumference
- Puskesmas: Pusat Kesehatan Masyarakat (Public Health Center)
- RMR: Resting Metabolic Rate; energy required by the body in a resting condition
- TMT-A/B: Trail Making Test Part A/B; cognitive function test
- WAZ: Weight for Age Z-score

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