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Socioeconomic status, remoteness, and tracking of nutritional status from childhood to adulthood in an Australian Aboriginal Birth Cohort ? the ABC study.

Journal:	BMJ Open
Manuscript ID	bmjopen-2019-033631
Article Type:	Research
Date Submitted by the Author:	14-Aug-2019
Complete List of Authors:	Sjöholm, Pauline; University of Turku, Department of Medicine Pahkala, Katja; University of Turku, Research Centre of Applied and Preventive Cardiovascular Medicine; University of Turku, Paavo Nurmi Centre, Sports & Exercise Medicine Unit, Department of Physical Activity and Health Davison, Belinda; Menzies School of Health Research Juonala, Markus; University of Turku, Department of Medicine; Murdoch Childrens Research Institute Singh, Gurmeet; Menzies School of Health Research; Flinders University, Northern Territory Medical Program
Keywords:	SOCIAL MEDICINE, PUBLIC HEALTH, Community child health < PAEDIATRICS, NUTRITION & DIETETICS, EPIDEMIOLOGY

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Socioeconomic status, remoteness, and tracking of nutritional status from childhood to adulthood in an Australian Aboriginal Birth Cohort – the ABC study.

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This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Conflicts of interest: The authors report no relationships that could be construed as a conflict of interest.

Contributorship statement: P.S., K.P., B.D., G.S. and M.J. contributed to the design and implementation of the research as well as the analysis and interpretation of data. B.D. and G.S. contributed to acquisition and management of data for the work. P.S. wrote the paper with input from all authors. All authors approved of the final version to be submitted and agree to be accountable for all aspects of the work.

Funding: The authors received no specific funding for this paper

Data sharing statement: All data are stored confidentially and are not freely available in the public domain, but specific proposals for collaboration are welcomed. Collaborations are established through formal agreement with the steering committee. Contact information: abcstudy@menzies.edu.au

Ethics statement: This study was approved by the Human Research Ethics Committee of Northern Territory Department of Health and Menzies School of Health Research, including the Aboriginal Ethical Sub-committee which has the power of veto (ABC Reference no. 2013-2022 and TEC Reference no. 2013-1986). All research was performed in accordance with the National Health and Medical Research Council guidelines (National Statement on Ethical Conduct in Human Research, 2008). Informed written consent was obtained from all participants.

Key words: Nutritional Status, Indigenous, Socioeconomic

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ABSTRACT

Objectives: To determine prevalences of underweight and overweight as well as low and high waist-to-height ratio (WHtR) in three prospective follow-ups and to explore tracking of these measures of nutritional status from childhood to adolescence and adulthood. The influence of socioeconomic status, remoteness, maternal body mass index (BMI) and birth weight on weight status was assessed.

Design: Longitudinal birth cohort study of Aboriginal Australians.

Setting: Data derived from three follow-ups of the Aboriginal Birth Cohort (ABC) study with mean ages of 11.4, 18.2 and 25.4 years for the participants.

Participants: Of the 686 Aboriginal babies recruited to the study between 1987-1990, 315 had anthropometric measurements for all three follow-ups and were included in this study.

Primary and secondary outcome measures: Categories for BMI (underweight, normal weight, overweight and obesity) and WHtR (low and high), sex, areal socioeconomic disadvantage as defined by the Indigenous Relative Socioeconomic Oucomes index, urban/remote residence, maternal BMI, birth weight. Logistic regression was used to calculate odds ratios for belonging to a certain BMI category in adolescence and adulthood according to BMI category in childhood and adolescence.

Results: Underweight was common (38% in childhood and 24% in adulthood) and the prevalence of overweight/obesity increased with age (12% in childhood and 35% in adulthood). Both extremes of weight status as well as low and high WHtR tracked from childhood to adulthood. Underweight was more common and overweight less common in remote and more disadvantaged areas. Birth weight and maternal BMI were associated with later weight status. There were significant sex differences for prevalences and tracking of WHtR but not for BMI.

Conclusions: Socioeconomic factors, remoteness and gender must be addressed when assessing nutrition-related issues in the Aboriginal communities due to the variation in nutritional status and its behaviour over time within the Aboriginal population.

ARTICLE SUMMARY

Strengths and limitations of this study

- This cohort is the longest-running and largest Indigenous birth cohort in Australia and presents unique data about the health of the contemporary Aboriginal population.
- Despite logistic challenges relating to geography, accessibility and cultural issues, the retention rates were good.
- The present study offers novel findings about the geographical, socioeconomic and gender differences in nutritional status that should be addressed when developing new strategies to reduce the immense health inequalities in Australia.
- The study population was relatively small with a substantial amount of missing data.
- Morbidity and clinical events related to nutritional status remain to be analysed later as the participants were still young adults during the last follow-up.



INTRODUCTION

The dual burden of simultaneous occurrence of obesity and underweight is a phenomenon commonly seen in low and middle-income countries but less so in high-income countries.[1] The Aboriginal population in Australia has experienced a dramatic nutritional transition since European colonisation.[2] Indigenous Australians, especially those living in remote regions, are prone to a number of morbidities associated with non-favourable nutrition throughout life.[3] In 2012-2013, Indigenous Australians were 1.5 times as likely to be affected by obesity as non-Indigenous Australians, with 30% of Indigenous children aged 2-14 years and 66% of persons aged 15 and over being affected by overweight or obesity.[4] On the other hand, 8% of Indigenous children were underweight compared with 4.8% of non-Indigenous children.[5] Obesity is a well documented risk factor for cardiovascular disease, type 2 diabetes, cancer and several other noncommunicable diseases.[6-7] Underweight, a possible manifestation of malnutrition and nutritional deficiencies, [8] is also associated with raised infection risk [9] and pregnancy complications. [10] Both extremes of body composition are associated with substantial medical costs for the communities involved.[11] Overweight and obesity tend to 'track' from childhood to adulthood, i.e. remain relatively stable throughout an individual's lifecourse, according to studies conducted in non-Indigenous populations.[12] There is a paucity of data in Aboriginal children and adolescents, not only regarding tracking of nutritional status but also about which anthropometric measures and cut-off points are most appropriate to define weight status for this population. Tracking of underweight is a topic less studied, but has been reported in some cohorts.[13]

Low socioeconomic status has been shown to be associated with obesity in several high-income countries.[14] In low and middle income countries, the association is often reversed, and persons of

higher socioeconomic status are more likely to be affected by obesity.[15] Little is known about the association of socioeconomic status and weight status within indigenous populations.

The Aboriginal Birth Cohort (ABC) was formed to better understand the reasons behind the high burden of disease of the Australian Aboriginal population and identify possibilities for early prevention. To date, the study is one of the longest running and largest Indigenous cohorts in the world. The intention of this paper is 1) to explore tracking of nutritional status from childhood to adulthood and 2) to explore the association of socioeconomic status and remoteness at birth with later nutritional status in the cohort.

METHODS

Participants

Details of the recruitment and follow-up of the ABC have been previously published in detail.[16-17] Between 1987 and 1990, 686 of the eligible 1238 babies born to Aboriginal mothers at the Royal Darwin Hospital were recruited into the study. There were no differences for mean birth weights or sex ratios between those recruited and those not recruited. To date, three follow-ups have been conducted: in childhood (mean age 11.4 years), adolescence (mean age 18.2 years) and most recently in early adulthood (mean age 25.4 years). The last follow-up took place in 2014-2016 and 70.9% of living participants were examined. All procedures contributing to this work comply with the Helsinki Declaration of 1975, as revised in 2008. All participants provided written informed consent to participate in this study, and all procedures were approved by the Human Research Ethics Committee of the Northern Territory Department of Health and the Menzies School of Health Research, including the Aboriginal Ethical Sub-committee which has the power of veto.

Patient and public involvement

The study has clear commitment to engaging with Indigenous communities, recruiting community members as assistants and building Indigenous capacity, encouraging and facilitating formal research training. Extensive consultation was conducted prior to each follow-up to obtain advice on contact methods, acceptability of planned procedures and methods of feedback to individuals and communities. This consultation process involved expert, cultural and cohort reference groups. Due to the difficulty in providing individual feedback except in limited circumstances, feedback is aimed at the communities. Updates are published in community newsletters and in the national Aboriginal and Islander Health Worker Journal and provided to local community groups.

Anthropometric measurements

Participants were categorised in classes of nutritional status using two alternative classifications: Body mass index (BMI), a widely used estimate for defining weight status and waist-to-height ratio (WHtR), an alternative anthropometric measure to define adiposity. WHtR has been suggested as a tool for better identifying abdominal obesity and delineating risk for cardiovascular disease and type 2 diabetes.[18] A cut-off value of 0.5 for WHtR has been commonly used for screening for cardio-metabolic risk irrespective of age, gender and ethnicity.[19–21] There is no consensus on a lower normal limit for WHtR, but a value of less than 0.4 has also been previously used.

At all follow-ups, weight was measured in light clothing while barefoot to the last complete 0.1 kg with a digital scale (TBF-521; Tanita Corporation, Arlington Heights, Illinois, USA). Height was measured with a portable stadiometer to the nearest millimetre using standardised procedures. BMI was calculated as weight (kg) divided by height (m) squared. Waist circumference was measured to the nearest millimeter using a flexible tape measure at the midpoint between the lowest rib and iliac crest at the end of expiration. WHtR was calculated as weight circumference in meters divided by

height in meters and categorised as low (<0.4), normal (0.4-0.49) or high (\geq 0.5).[22] For participants who had attained 18 years at follow-up, following BMI values for categories of weight status were used: <18,5: underweight, 18.5-24.99: normal weight, 25-29.99: overweight, \geq 30: obesity. For participants who were under 18 years of age at the time of the follow-up, specific age and sex specific cut-off points were used for categories of weight status (underweight, normal weight, overweight and obesity) as defined by the International Obesity Task Force.[23-24] Participants who were pregnant at follow-up (N=26) were left out of analyses. Only participants who had both height, weight and waist circumference recorded at all follow-ups were included (N=315).

Remoteness and childhood socioeconomic situation

For areal socioeconomic disadvantage, the Indigenous Relative Socioeconomic Outcomes (IRSEO) index was used. It is a score calculated at the Indigenous Area level and it is based on 9 variables, 3 related to employment, 3 to education, 2 to housing and 1 to income, using information from the 2011 Census of Population and Housing. Each area is assigned to one of 100 percentiles, 1 for the most advantaged and 100 for the most disadvantaged.[25] Based on their reported addresses at birth, the participants were assigned an IRSEO score. The scores were categorised into three groups: low disadvantage (range 13 to 37), mid-high disadvantage (range 43 to 89), and high disadvantage (range 91 to 99).

Families living in urban areas at birth were classified as urban and those in remote locations as nonurban. Maternal BMI was recorded at birth and classified as underweight (< 18.5), normal weight (18.5-24.99), overweight (25-29.99) or obese (\geq 30). Birthweight of the participants was transformed into Z-scores and put into 5 categories.

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Statistical analyses

Tracking of weight status was analysed using logistic regression and defining the odds ratio (OR) of belonging to a certain weight class in adolescence and adulthood according to weight class in childhood and adolescence. Regression analyses were adjusted for age at later follow-up, sex and time between compared follow-ups. Overweight and obesity were combined into one category due to small numbers.

Chi-square tests were used to assess the association of weight status and categories of remoteness, socioeconomic status, maternal BMI and birth weight. Attrition analyses were performed to compare baseline characteristics between participants and non-participants of the follow-ups with t-tests for continuous and chi-square tests for categorical variables.

Statistical tests were performed with SAS version 9.4 (SAS Institute, Inc, Cary, NC). Statistical significance was inferred at a 2-tailed P-value < 0.05.

Results

Descriptive statistics of the participants are presented in table 1 and results from the attrition analysis are reported in supplementary table 1. There were significant differences between participants and dropouts regarding remoteness and areal disadvantage: dropouts were more often urban residents and came from less disadvantaged areas according to IRSEO scores. There were no differences regarding sex, birth weight and maternal BMI.

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Anthropometric characteristics of participants

	Child	hood	Adoles	cence	Adulthood		
	Male	Female	Male	Female	Male	Female	
Age, years ± SD	11.1 ± 1.1	10.8 ± 1.1	17.9 ± 1.1	17.7 ± 1.1	25.4 ± 1.1	25.2 ± 1.2	
Weight, kg	34.3 ± 11.5	35.2 ± 11.5	64.1 ± 20.2	53.7 ± 13.0	71.1 ± 21.2	60.6 ± 16.0	
Height, cm	143.1 ± 10.1	143.0 ± 10.5	173.3 ± 6.9	161.3 ± 5.2	174.3 ± 7.0	161.4 ± 5.6	
BMI	16.4 ± 3.5	16.8 ± 3.4	21.2 ± 5.6	20.7 ± 4.9	23.3 ± 6.0	23.3 ± 6.2	
Waist circumference, cm	63.8 ± 9.5	63.9 ± 9.0	78.8 ± 14.5	77.7 ± 12.6	85.7 ± 16.0	86.2 ± 15.1	
WHtR	0.45 ± 0.05	0.45 ± 0.05	0.45 ± 0.08	0.48 ± 0.08	0.49 ± 0.09	0.54 ± 0.1	

Early life characteristics of participants

	Male	Female	Total
Ν	158 (50.2%)	157 (40.8%)	315
Urban residence, %	13.3	8.3	10.8 (N=315)
Birth weight, Z score ± SD	-0.16 ± 1.2	-0.42 ± 1.1	-0.29 ± 1.1 (N=293)
IRSEO score	78.6 ± 23.9	83.0 ± 19.7	80.8 ± 22.0 (N=315)
BMI of mother	22.0 ± 3.8	22.6 ± 4.4	22.3 ± 4.1 (N=236)

Table 1. Descriptive characteristics. Mean values with standard deviations for anthropometric measurements of participants in three follow-ups and baseline characteristics.

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Prevalences of BMI derived weight classes according to sex are presented in figure 1. There were no significant differences between the sexes in the prevalence of underweight, overweight or obesity. For both sexes, the combined prevalence of underweight was 38.1 % in childhood, 38.1 % in adolescence and 23.5 % in adulthood. The respective prevalences for overweight were 8.9 %, 12.1% and 22.9 %, and for obesity 2.9 %, 6.4 % and 11.8 %.

Prevalences of low (<0.4) and high (≥ 0.5) WHtR in the three follow-ups are presented in figure 2. There were no differences between the sexes in childhood. In later follow-ups, male participants more often had a low WHtR (22.2 vs. 10.2 % in adolescence [P=0.004] and 13.9 vs. 5.1 % in adulthood [P=0.008]) while female participants more often had a high WHtR (34.4 vs. 20.9 % in adolescence [P=0.007] and 58.6 vs. 36.1 % in adulthood [P<0.0001]).

The associations between weight class and urban residence, maternal BMI, areal disadvantage (IRSEO) and birth weight are presented in figure 3. Urban participants were more often affected by overweight/obesity and were less often underweight than non-urban participants in all follow-ups. Maternal weight status was significantly associated with offspring weight status in all follow-ups with children of underweight mothers being more often underweight and children of mothers affected by overweight and obesity more often presenting with overweight and obesity. Areal socioeconomic disadvantage was associated with weight class in all follow-ups: participants from more disadvantaged areas were more often underweight and less often presented with overweight/obesity than participants from less disadvantaged areas. Birth weight was also associated with later weight status: smaller babies were more often underweight and were less often affected by overweight or obesity in all follow-ups.

Analyses of tracking of weight status according to BMI categories are presented in table 2. Tracking was significant between age groups for all BMI categories and sex was not a significant confounder in any of the analyses. Of the participants who were affected by overweight/obesity in childhood, 67.6% remained in the same weight status category in adolescence (OR 16.0, P < 0.0001) and

> 83.8% in adulthood (OR 9.8, P < 0.0001). Of the adolescents affected by overweight/obesity, 86.2% were affected by overweight/obesity as adults (OR 22.5, P < 0.0001). Underweight status was also significantly stable throughout the follow-ups. Of the participants who were underweight in childhood, 76.7% were underweight in adolescence (OR 22.6, P < 0.0001) and 46.7% remained underweight in adulthood (OR 9.8, P < 0.0001). Of underweight adolescents, 83.8% were underweight in adulthood (OR 17.3, P < 0.0001).

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² **Table 2.** Associations between weight classes at different timepoints ³

4 5			Ado	lescence						Adu	lthood		
6			Underweight			erweight/obese		Underweight			Overweight/obese		
7													
8		%	OR (CI)	P-value	%	OR(CI)	P-value	%	OR (CI)	P-value	%	OR (CI)	P-value
9 Childhood	Underweight	76.7%	22.6 (12.2-42.0)	<0.0001	0%	-	-	46.7%	9.8 (5.2-18.6)	< 0.0001	8.3%	0.09 (0.04-0.2)	<0.0001
10 11	Normal weight	17.7%	0.15 (0.09-0.3)	<0.0001	20.9%	1.4 (0.8-2.5)	0.25	10.8%	0.2 (0.1-0.4)	<0.0001	43.0%	2.1 (1.3-3.5)	0.002
12	Overweight/obese	0%		-	67.6%	16.0 (7.1-35.7)	< 0.0001	2.7%	0.07 (0.009-0.5)	0.0095	83.8%	13.2 (5.3-33.0)	<0.0001
13 Adolescence 14	Underweight	-	- O,	-	-	-	-	83.8%	17.3 (8.5-35.2)	<0.0001	3.3%	0.03 (0.009-0.08)	<0.001
14	Normal weight	-	-	5	-	-	-	16.2%	0.2 (0.09-0.34)	<0.0001	40.2%	1.6 (0.98-2.5)	0.06
16 17	Overweight/obese	-	-	20	-	-	-	0%	-	-	86.2%	22.5 (10.0-51.0)	<0.0001

18

20 Tracking of weight classes from childhood and adolescence to adolescence and adulthood, eg. of the children who were underweight at first follow-up, 76.7% remained underweight in adolescence and 46.7 % in adulthood. Weight classes for participants < 18 years of age based on age and sex specific BMI cut-off points according to Cole et al. (2000, 2007). For adults: underweight BMI < 18.5; normal weight BMI 18.5-24.99; overweight/obese BMI ≥ 2125. OR adjusted for age (years) at earlier follow-up, time (years) between follow-ups and sex. % indicates percent of participants in weight class at later follow-up.

There was significant tracking of both low and high WHtR in all follow-ups with sex being a significant confounder in most analyses (table 3). Of the children who had a low WHtR, 44.7% remained in the same category in adolescence (OR 6.9, P < 0.0001) and 23.7% in adulthood (OR 4.5, P=0.001) while 46.7% of adolescents with a low WHtR had a low WHtR in adulthood (OR 45.1, P < 0.0001). Of the children with a high WHtR, 71.1% had a high WHtR in adolescence (OR 9.3, P<0.0001) and 94.7% in adulthood (OR 28.6, P < 0.0001). Of adolescents with a high WHtR, 85.1% remained in the same category in adulthood (OR 11.3, P<0.0001).

Table 3. Associations between low and high WHtR at different time points

6																					
7			Adolescence									Adulthood									
8 9				WHtR < 0.	4				WHtR ≥ 0.5					WHtR < 0	.4				WHtR ≥ 0.	5	
10		%	OR (CI)	P-value	OR for sex	P-value for sex	%	OR(CI)	P-value	OR for sex	P-value for sex		OR (CI)	P-value	OR for sex	P-value for sex	%	OR(CI)	P-value	OR for sex	P-value for sex
11 Childhood	WHtR < 0.4	44.7	6.9 (3.2-15.1)	<0.0001	3.2 (1.6-6.4)	0.001	2.6	0.05 (0.007-0.4)	0.004	0.4 (0.3-0.7)	0.002	23.7	4.5 (1.8-11.4)	0.001	3.5 (1.5-8.6)	0.005	21.1	0.2 (0.1-0.5)	0.0005	0.4 (0.2-0.6)	<0.0001
12 13	WHtR ≥ 0.5	0.0	-	-	-	-	71.1	9.3 (4.2-20.4)	<0.0001	0.5 (0.3-0.8)	0.005	0.0	- 26.7 (10.3-	-	-	-	94.7	28.6 (6.6-122.9)	<0.0001	0.4 (0.2-0.6)	<0.0001
A dd plescence	WHtR < 0.4	-	-	-	-	-	-	-	-	-	-	45.1	69.2)	<0.0001	2.0 (0.8-5.3)	0.2	9.8	0.1 (0.04-0.3)	<0.0001	0.5 (0.3-0.7)	0.001
15 16	WHtR ≥ 0.5	-	-	-	-	-	-	· /	-	-	-	0.0	-	-	-	-	85.1	11.3 (5.8-21.9)	<0.0001	0.5 (0.3-0.8)	0.003
16																					

Tracking of waist-to-height ratio from childhood and adolescence to adolescence and adulthood. OR adjusted for age (years) at earlier follow-up, time (years) between follow-ups and sex. OR for sex modeled as male Vs8 female. % indicates per cent of participants in WHtR at later follow-up.

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DISCUSSION

The present study shows that there is significant tracking of nutritional status from childhood to adulthood among Indigenous Australians in this cohort, both when assessed with BMI or with WHtR categories. In contrast to BMI, there were significant differences between the sexes for both tracking and prevalence of WHtR categories with females more often presenting with central adiposity in adolescence and adulthood. This finding is consistent with previous studies that show that Aboriginal women in general have greater waist circumference than their non-Aboriginal counterparts.[26-27] We have previously found that females in this cohort have lower levels of physical activity, which may be a possible contributing factor.[28] Central adiposity is a known risk factor for cardiovascular morbidity which accounts for a substantial part of the disparity in health outcomes between Indigenous and non-Indigenous Australians. Therefore, women seem to be at particular risk for chronic disease due to their body fat composition.[27]

Both areal disadvantage and non-urban residence were associated with lower prevalence of overweight/obesity and higher rates of underweight. This is in contrast to a study from New South Wales, where Aboriginal people from more advantaged and urban surroundings had lower prevalences of obesity and overweight than those from remote and disadvantaged areas.[29] It seems that the spatial trend in obesity in this cohort is similar to that traditionally seen in low and middle income countries, where obesity is more concentrated in cities and wealthier regions and underweight is more common in remote and rural settings. [5] The dual burden of malnutrition and the urban-remote differential in nutritional status has been previously described in the cohort at an average age of 25 years.[30]

The association between maternal BMI and offspring BMI is consistent with previous studies. In the Generation R study, it was found that maternal obesity is associated with adverse cardiometabolic risk profiles including obesity, higher systolic blood pressure and adverse lipid levels in the offspring.[31] In the Avon Longitudinal Study of Parents and Children (ALSPAC), a

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linear trend between maternal pre-pregnancy BMI and offspring adiposity levels was found: offspring of underweight mothers had lower rates and offspring of overweight mothers had higher rates of adiposity. DNA methylation was suggested as a mediating factor.[32]

From a public health point of view, the present paper presents further evidence that dietary interventions need more tailored approaches, as there exist large variations within the Aboriginal community regarding nutritional status and its behaviour over time. Interventions need to be delivered within critical time windows and the gender perspective is essential: pre-pregnant women and girls in general should receive special attention.[33] Nutrition education has been reported to have some positive effect on obesity in Aboriginal communities[34], but novel approaches are needed and the focus should be placed on the most affected and vulnerable members of the communities. Increasing the levels of physical activity, especially in girls, may be a key factor.

The strengths of the study include its longitudinal design and well-structured follow-ups with relatively good retention rates. The study population however is relatively small causing some limitations to the interpretation of the results and as only participants with data from all follow-ups were included, the missing data was quite substantial. There were significant differences between participants and non-participants, as participants were more often from non-urban and more disadvantaged areas. The presented associations between weight status and socioeconomic status, remoteness, maternal BMI and birth weight are merely descriptive analyses presented separately for each follow-up as the data was not analysed in a longitudinal fashion and correlation over time was not assessed as this was not the main aim of the article. Other limitations include the definition of socioeconomic status, as the individual level indicators of socioeconomic status such as income were not available. IRSEO describes socioeconomic disadvantage on an area level and may not reflect the individual situation of the participants. Finally, the participants were still young during the last follow-up. After future follow-ups, cardiovascular morbidity and clinical events are likely to

be more prevalent and could be analysed for even better understanding of the clinical relevance of the nutritional status and obesity trends in this cohort.

In summary, the present study presents evidence on tracking of nutritional status from childhood to adulthood in this unique Aboriginal cohort. Socioeconomic status and remoteness factors were associated with weight status in all follow-ups. The differences in central adiposity between males and females that seem to arise after childhood indicate a need for targeted and successfully timed approaches in dietary interventions.

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FIGURE LEGENDS

Figure 1. Percentages of underweight and overweight/obese participants by sex. For classification, age and sex specific cut-off points were used for participants under 18 years of age at follow-up. For participants aged 18 and over, underweight was classified as BMI < 18,5; normal weight as 18,5-24,99; overweight as 25-29,99 and obesity as \geq 30.

Figure 2. Prevalences for low and high waist-to-height ratio at three time points according to sex. P-values are calculated with chi-square tests and represent differences between sexes. Values are in percentages.

Figure 3. Prevalences of overweight/obesity and underweight in participants according to urban residence (A), maternal BMI (B), areal disadvantage (C), and birth weight (D). Chi-square tests were used to assess association between weight status and presented categories.

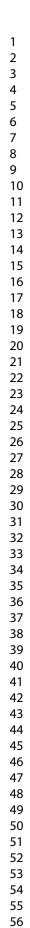
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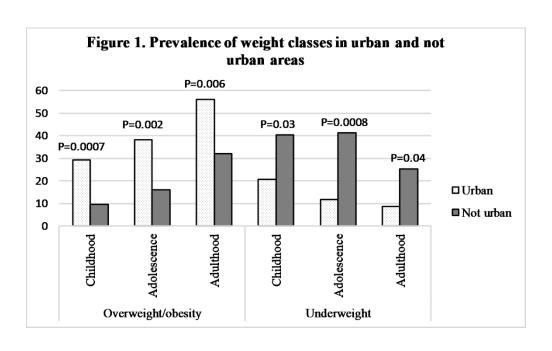
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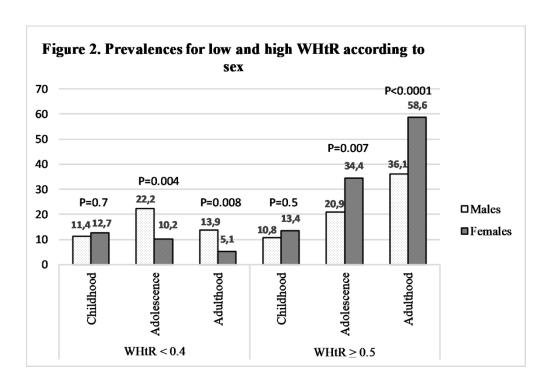
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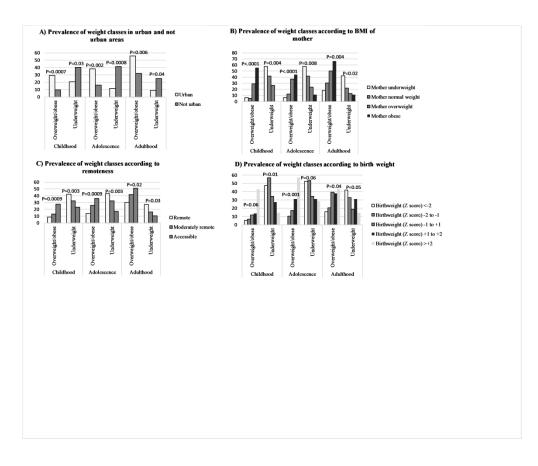
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Supplementary table 1. Attrition analysis.

5 6 7		Participants (N=315)	Dropouts (N=371)	P-value
8 9	Males (%)	50.2	53.1	P=0.44
10	Urban residence (%)	10.8	31.8	P<0.0001
11	Birthweight, z score	-0.29	-0.30	P=0.95
12	IRSEO score	80.8	65.9	P<0.0001
13 14	Maternal BMI	22.2	22.3	P=0.71

Comparison between participants and dropouts. Values for categorical variables (sex, urban residence) are presented in percentages and values for continuous variables in means. Chisquare tests were used for analysis of categorical variables an ttests for continuous variables.

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STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the	2
		abstract	
		(b) Provide in the abstract an informative and balanced summary of what was	2
		done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods		State specific objectives, merading any prespectived hypotheses	
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of	5
8		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of	5
I	-	participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and	
		unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	6-7
		effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	6-7
measurement		assessment (measurement). Describe comparability of assessment methods if	
		there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	5, 12
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,	6-7
		describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for	8
		confounding	
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, explain how loss to follow-up was addressed	
		(<u>e</u>) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially	5
		eligible, examined for eligibility, confirmed eligible, included in the study,	
		completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	table
		and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	table

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Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their	8-10
		precision (eg, 95% confidence interval). Make clear which confounders were adjusted for	
		and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a	
		meaningful time period	
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity	
		analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-
			11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.	12
		Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,	11-
		multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12

 Other information

 Funding
 22
 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based
 1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Socioeconomic status, remoteness, and tracking of nutritional status from childhood to adulthood in an Australian Aboriginal Birth Cohort - the ABC study.

Journal:	BMJ Open
Manuscript ID	bmjopen-2019-033631.R1
Article Type:	Research
Date Submitted by the Author:	25-Nov-2019
Complete List of Authors:	Sjöholm, Pauline; University of Turku, Department of Medicine Pahkala, Katja; University of Turku, Research Centre of Applied and Preventive Cardiovascular Medicine; University of Turku, Paavo Nurmi Centre, Sports & Exercise Medicine Unit, Department of Physical Activity and Health Davison, Belinda; Menzies School of Health Research Juonala, Markus; University of Turku, Department of Medicine; Murdoch Childrens Research Institute Singh, Gurmeet; Menzies School of Health Research; Flinders University, Northern Territory Medical Program
Primary Subject Heading :	Nutrition and metabolism
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	SOCIAL MEDICINE, PUBLIC HEALTH, Community child health < PAEDIATRICS, NUTRITION & DIETETICS, EPIDEMIOLOGY

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Socioeconomic status, remoteness, and tracking of nutritional status from childhood to adulthood in an Australian Aboriginal Birth Cohort – the ABC study.

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This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Northern Territory Medical Program, Flinders University, Darwin, Australia

Conflicts of interest: The authors report no relationships that could be construed as a conflict of interest.

Contributorship statement: P.S., K.P., B.D., G.S. and M.J. contributed to the analysis and interpretation of data. B.D. and G.S. were responsible for the design and implementation of the larger study of which this paper is a part. B.D and G.S. collected and managed the data used in this study. P.S. wrote the paper with input from all authors. All authors approved of the final version to be submitted and agree to be accountable for all aspects of the work.

Funding: The authors received no specific funding for this paper

Data sharing statement: All data are stored confidentially and are not freely available in the public domain, but specific proposals for collaboration are welcomed. Collaborations are established through formal agreement with the ABC steering committee. Contact information: abcstudy@menzies.edu.au

Ethics statement: This study was approved by the Human Research Ethics Committee of Northern Territory Department of Health and Menzies School of Health Research, including the Aboriginal Ethical Sub-committee which has the power of veto (ABC Reference no. 2013-2022). All research was performed in accordance with the National Health and Medical Research Council guidelines (National Statement on Ethical Conduct in Human Research, 2008). Informed written consent was obtained from all participants.

Key words: Nutritional Status, Indigenous, Socioeconomic

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ABSTRACT

Objectives: To determine prevalences of underweight and overweight as well as low and high waist-to-height ratio (WHtR) in three prospective follow-ups and to explore tracking of these measures of nutritional status from childhood to adolescence and adulthood. The influence of socioeconomic status, remoteness, maternal body mass index (BMI) and birth weight on weight status was assessed.

Design: Longitudinal birth cohort study of Indigenous Australians.

Setting: Data derived from three follow-ups of the Aboriginal Birth Cohort (ABC) study with mean ages of 11.4, 18.2 and 25.4 years for the participants.

Participants: Of the 686 Indigenous babies recruited to the study between 1987-1990, 315 had anthropometric measurements for all three follow-ups and were included in this study.

Primary and secondary outcome measures: Categories for BMI (underweight, normal weight, overweight and obesity) and WHtR (low and high), sex, areal socioeconomic disadvantage as defined by the Indigenous Relative Socioeconomic Oucomes index, urban/remote residence, maternal BMI, birth weight. Logistic regression was used to calculate odds ratios for belonging to a certain BMI category in adolescence and adulthood according to BMI category in childhood and adolescence.

Results: Underweight was common (38% in childhood and 24% in adulthood) and the prevalence of overweight/obesity increased with age (12% in childhood and 35% in adulthood). Both extremes of weight status as well as low and high WHtR tracked from childhood to adulthood. Underweight was more common and overweight less common in remote and more disadvantaged areas. Birth weight and maternal BMI were associated with later weight status. There were significant sex differences for prevalences and tracking of WHtR but not for BMI.

Conclusions: Socioeconomic factors, remoteness and gender must be addressed when assessing nutrition-related issues in the Indigenous communities due to the variation in nutritional status and its behaviour over time within the Indigenous population.

ARTICLE SUMMARY

Strengths and limitations of this study

- This cohort is the longest-running and largest Indigenous birth cohort in Australasia and presents unique data about the health of the contemporary Indigenous population.
- Despite logistic challenges relating to geography and accessibility, the retention rates were good.
- The present study offers novel findings about the geographical, socioeconomic and gender differences in nutritional status that should be addressed when developing new strategies to reduce the immense health inequalities in Australia.
- The study population was relatively small with a substantial amount of missing data.
- At this young age, the participants are healthy with very few showing overt disease, thus analysis of morbidity was not done. This will be addressed in future follow-ups.

L'AND

INTRODUCTION

The dual burden of simultaneous occurrence of obesity and underweight is a phenomenon commonly seen in low and middle-income countries but less so in high-income countries.[1] The Indigenous (used respectfully to include both Aboriginal and Torres Strait Islander peoples) population in Australia has experienced a dramatic nutritional transition since European colonisation.[2] Indigenous Australians, especially those living in remote regions, are prone to a number of morbidities associated with non-favourable nutrition throughout life.[3] In 2012-2013, Indigenous Australians were 1.5 times as likely to be affected by obesity as non-Indigenous Australians, with 30% of Indigenous children aged 2-14 years and 66% of persons aged 15 and over being affected by overweight or obesity.[4] On the other hand, underweight was almost twice as common in childhood: 8% of Indigenous children were underweight compared with 4.8% of non-Indigenous children.[5] Obesity is a well documented risk factor for cardiovascular disease, type 2 diabetes, cancer and several other non-communicable diseases, [6-7] while underweight, a possible manifestation of malnutrition and nutritional deficiencies,[8] is also associated with raised infection risk[9] and pregnancy complications.[10] Both extremes of body composition are associated with substantial medical costs for the communities involved.[11] Overweight and obesity tend to 'track' from childhood to adulthood, i.e. remain relatively stable throughout an individual's lifecourse, according to studies conducted in non-Indigenous populations.[12] Tracking of underweight is a topic less studied, but has been reported in some cohorts.[13] There is a paucity of data in Indigenous children and adolescents regarding tracking of nutritional status.

In high-income countries, low socioeconomic status has been shown to be associated with obesity.[14] However, in low and middle income countries, the association is often reversed, and

persons of higher socioeconomic status are more likely to be affected by obesity.[15] The effects of socioeconomic factors and remoteness on nutritional status have generally been similar for the Indigenous and the non-Indigenous Australians with obesity being concentrated in urban and less disadvantaged areas.[4,16] To our knowledge, there have been no studies examining the longitudinal development of nutritional status and its associations with socioeconomic factors in very remote regions of Australia, where food insecurity is high [17] and malnutrition and underweight are more common.[18]

The Aboriginal Birth Cohort (ABC) was formed to better understand the reasons behind the high burden of disease of the Australian Indigenous population and identify possibilities for early prevention. To date, the study is one of the longest running and largest Indigenous birth cohorts in Australasia. The intention of this paper is 1) to explore tracking of nutritional status from childhood to adulthood and 2) to explore the association of socioeconomic status and remoteness at birth with elez on later nutritional status in the cohort.

METHODS

Participants

Details of the recruitment and follow-up of the ABC have been previously published in detail.[19-20] In brief, between 1987 and 1990, 686 of the eligible 1238 babies born to Indigenous mothers at the Royal Darwin Hospital were recruited into the study. There were no differences for mean birth weights or sex ratios between those recruited and those not recruited. Since recruitment (Wave-1), three follow-ups have been conducted: in childhood (Wave-2) at a mean age of 11.4 years (n=572; 86 % of living participants), in adolescence (Wave-3) at a mean age of 18.2 years (n=469; 71 % of living participants) and most recently in early adulthood (Wave-4) at a mean age of 25.4 years (n=459; 71 % of living participants).

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All procedures contributing to this work comply with the Helsinki Declaration of 1975, as revised in 2008. All participants provided written informed consent to participate in this study, and all procedures were approved by the Human Research Ethics Committee of the Northern Territory Department of Health and the Menzies School of Health Research, including the Aboriginal Ethical Sub-committee which has the power of veto.

Patient and public involvement

The study has clear commitment to engaging with Indigenous communities and building Indigenous capacity. Indigenous researchers have been involved in all aspects of the study at each of the follow-ups including investigators, data collection team and local community members employed as research assistants, encouraging and facilitating formal research training. Extensive consultation with expert, Indigenous and cohort reference groups was conducted prior to each follow-up to obtain advice and guidance on contact methods, acceptability of planned procedures and methods of feedback to individuals and communities. Due to the difficulty in providing individual feedback after the initial visit, feedback is aimed at the community level in remote areas. Updates are published in community newsletters and in the national Aboriginal and Islander Health Worker Journal and provided to local community groups.

Anthropometric measurements

At birth, maternal height and weight was recorded and used to calculate body mass index (BMI; kg/m²) which was classified as underweight (< 18.5), normal weight (18.5-24.99), overweight (25-29.99) or obese (\geq 30). Birthweight of the participants was transformed into Z-scores and put into 5 categories based on the WHO child growth charts [21] 1) low: <-2; 2) low-normal: -2 to -1; 3) normal: -1 to 1; 4) normal-high: 1 to 2; and 5) high >2.

At each follow-up of the study, a small group (3-4) of trained researchers measured height and weight using standardized methods. Weight was measured in light clothing while barefoot to the last complete 0.1 kg with a digital scale (TBF-521; Tanita Corporation, Arlington Heights, Illinois, USA). Height was measured with a portable stadiometer to the nearest millimeter. BMI was calculated as weight (kg) divided by height (m) squared. Waist circumference was measured to the nearest millimeter using a flexible tape measure at the midpoint between the lowest rib and iliac crest at the end of expiration.

Participants were categorised in classes of nutritional status using two alternative classifications: Body mass index (BMI), a widely used estimate for defining weight status and waist-to-height ratio (WHtR), an alternative anthropometric measure to define adiposity.

For participants who had attained 18 years at follow-up, the following BMI categories were used: underweight <18,5, normal weight 18.5-24.99, overweight 25-29.99, obese \geq 30. For participants who were under 18 years of age at time of follow-up, age and sex specific cut-off points were used for categories of weight status (underweight, normal weight, overweight and obese) as defined by the International Obesity Task Force.[22-23]

WHtR has been suggested as a tool for better identifying abdominal obesity and delineating risk for cardiovascular disease and type 2 diabetes.[24] A cut-off value of 0.5 for WHtR has been commonly used for screening for cardio-metabolic risk irrespective of age, gender and ethnicity.[25-27] There is no consensus on a lower normal limit for WHtR, but a value of less than 0.4 has also been previously used. WHtR was calculated as waist circumference in centimeters divided by height in centimeters and categorised as low (<0.4), normal (0.4-0.49) or high $(\geq 0.5).[28]$

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Remoteness and childhood socioeconomic situation

For areal socioeconomic disadvantage, the Indigenous Relative Socioeconomic Outcomes (IRSEO) index was used. The IRSEO is calculated at the Indigenous Area level and is based on 9 variables, 3 related to employment, 3 to education, 2 to housing and 1 to income, using information from the 2011 Census of Population and Housing. Each area is assigned to one of 100 percentiles, 1 for the most advantaged and 100 for the most disadvantaged.[29] Based on their reported addresses at birth, the participants were assigned an IRSEO score. The scores were categorised into three groups: low disadvantage (1 to 40), mid-high disadvantage (range 41 to 90), and high disadvantage (range 91 to 100).

Area of residence was classified at birth, with families residing in a rural community with an Aboriginal council classified as "remote" and all "non-remote" locations were classified as "urban". At Wave-4, 18 % of participants reported to have lived in another community at some point in their lives. However, limited movement between urban and remote settings was seen, with 8.7 % of participants who had lived in a remote community at birth moving to an urban community by Wave-4 and 19 % of the participants who had lived in an urban community at Wave-2 moving to a remote location at by Wave-4.

Statistical analyses

Participants who were pregnant in Wave-3 and/or Wave-4 were excluded from the analyses. Only participants who had height, weight and waist circumference recorded at all follow-ups were included (N=315). Overweight and obesity were combined into one category due to small numbers. Attrition analyses were performed to compare baseline characteristics between participants included and not included at each follow-up with t-tests for continuous and chi-square tests for categorical

variables. Chi-square tests were used to assess the association of weight status and categories of remoteness, socioeconomic status, maternal BMI and birth weight at all follow-ups separately. Tracking of nutritional status (underweight, overweight/obese and WHtR, low and high) was analysed using logistic regression and reported as odds ratio (OR) of status being constant across time: status in childhood continuing into adolescence and adulthood and status in adolescence continuing into adulthood. Regression analyses were adjusted for age at follow-up, sex and time between compared follow-ups

To assess the changes over time, Cochran's Q tests and McNemar's tests were used to analyse the differences in the proportions of nutritional status categories by sex over the course of the three follow-ups.

Statistical tests were performed with SAS version 9.4 (SAS Institute, Inc, Cary, NC). Statistical significance was inferred at a 2-tailed P-value < 0.05.

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Results

Complete data (height, weight and waist circumference) at all follow-ups were available on 315 participants. There were no significant differences in sex, birth weight and maternal BMI in participants included and those not included. There were significant differences between the two groups regarding remoteness and areal disadvantage: those included were more from remote and more disadvantaged areas according to IRSEO scores (see supplementary table 1). There were no significant differences between the BMI or the WHtR values at any follow-up between participants included and those not included (for BMI: P=0.48 for Wave-2 and Wave-3, P=0.47 for Wave-4; for WHtR P=0.5, 0.46 and 0.52 respectively). Descriptive statistics of the participants are presented in table 1.

Anthropometric characteristics of participants

	Childhood	l (Wave-2)	Adolescenc	e (Wave-3)	Adulthood (Wave-4)		
	Male	Female	Male	Female	Male	Female	
Age, years ± SD	11.1 ± 1.1	10.8 ± 1.1	17.9 ± 1.1	17.7 ± 1.1	25.4 ± 1.1	25.2 ± 1.2	
Weight, kg	34.3 ± 11.5	35.2 ± 11.5	64.1 ± 20.2	53.7 ± 13.0	71.1 ± 21.2	60.6 ± 16.0	
Height, cm	143.1 ± 10.1	143.0 ± 10.5	173.3 ± 6.9	161.3 ± 5.2	174.3 ± 7.0	161.4 ± 5.6	
BMI	16.4 ± 3.5	16.8 ± 3.4	21.2 ± 5.6	20.7 ± 4.9	23.3 ± 6.0	23.3 ± 6.2	
Waist circumference, cm	63.8 ± 9.5	63.9 ± 9.0	78.8 ± 14.5	77.7 ± 12.6	85.7 ± 16.0	86.2 ± 15.1	
WHtR	0.45 ± 0.05	0.45 ± 0.05	0.45 ± 0.08	0.48 ± 0.08	0.49 ± 0.09	0.54 ± 0.1	

	Male	Female	Total
Ν	158 (50.2%)	157 (40.8%)	315
Urban residence, %	13.3	8.3	10.8 (N=315)
Birth weight, Z score ± SD	-0.16 ± 1.2	-0.42 ± 1.1	-0.29 ± 1.1 (N=293)
IRSEO score	78.6 ± 23.9	83.0 ± 19.7	80.8 ± 22.0 (N=315)
BMI of mother	22.0 ± 3.8	22.6 ± 4.4	22.3 ± 4.1 (N=236)

Table 1. Descriptive characteristics. Mean values with standard deviations for anthropometric measurements of participants in three follow-ups and baseline characteristics.

High rates of underweight were seen at all 3 follow-ups: 38.1 % at Wave-2, 38.1 % at Wave-3 and 23.5 % at Wave-4. Overweight and obesity increased over time: for overweight, 8.9 % at Wave-2, 12.1% at Wave-3 and 22.9 % at Wave-4, and for obesity, 2.9 %, 6.4 % and 11.8 % respectively. Prevalences of BMI categories according to sex are presented in figure 1. There were no significant differences between the sexes in the prevalence of underweight, overweight or obesity.

The differences in weight status over the course of the three follow-ups were significant (P<0.0001 for underweight and overweight/obesity for both sexes). There was no statistically significant difference in the rate of underweight between Wave-2 and Wave-3 (P=0.56 for males and P=0.76 for females) but a significant difference in the prevalence of underweight between Wave-2 and Wave-4 (P<0.0001 for both sexes) as well as between Wave-3 and Wave-4 (P<0.0001 for both sexes) as well as between Wave-3 and Wave-4 (P<0.0001 for both sexes). For the prevalences of overweight/obesity, there was a statistically significant difference between Wave-2 and Wave-3 for male participants but not for females (P=0.002 for males and P=0.16 for females). Between Wave-2 and Wave-4 the difference was statistically significant for both sexes (P<0.0001) as well as between Wave-3 and Wave-4 (P=0.0007 for males and P<0.0001 for both sexes).

Prevalences of low (<0.4) and high (≥ 0.5) WHtR in the three follow-ups are presented in figure 2. There were no differences between the sexes at Wave-2. In later follow-ups, male participants more often had a low WHtR (22.2 vs. 10.2 % at Wave-3 [P=0.004] and 13.9 vs. 5.1 % at Wave-4 [P=0.008]) while female participants more often had a high WHtR (34.4 vs. 20.9 % at Wave-3 [P=0.007] and 58.6 vs. 36.1 % at Wave-4 [P<0.0001]). The changes in WHtR over the course of the three follow-ups were significant (P=0.002 for males and P=0.03 for females for low WHtR and P<0.0001 for both sexes for high WHtR). Between Wave-2 and Wave-3, there was a statistically significant difference between the rates for low WHtR for males (P=0.003) but not for females (P=0.4). Between Wave-2 and Wave-4 the difference was significant for females (P=0.01) but not for males (P=0.4). For high WHtR, the difference was significant between Wave-2 and Wave-3

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(P=0.002 for males and P<0.0001 for females) and between Wave-2 and Wave-4 (P<0.0001 for both sexes).

The associations between weight class and remoteness, maternal BMI, areal disadvantage (IRSEO) and birth weight are presented in figure 3. Urban participants were significantly more likely to be overweight/obese and less likely to be underweight than remote participants in all follow-ups. Areal socioeconomic disadvantage was significantly associated with weight class in all follow-ups: participants from more disadvantaged areas were more often underweight and less often overweight/obese than participants from less disadvantaged areas. Maternal weight status was significantly associated with offspring weight status in all follow-ups with children of underweight mothers being more often underweight and children of overweight and obese mothers more often presenting with overweight and obesity. Birth weight was also associated with later weight status: smaller babies were more often underweight and less often overweight or obese in all follow-ups. The association was significant in all follow-ups except for overweight status at Wave-2 (P=0.06) and underweight status at Wave-3 (P=0.06).

Analyses of tracking of weight status according to BMI categories are presented in table 2. Tracking was significant between age groups for all BMI categories, with sex not a significant confounder in any of the analyses. Of the participants who were overweight/obese at Wave-2, 67.6% remained in the same weight status category at Wave-3 (OR 16.0, P < 0.0001) and 83.8% at Wave-4 (OR 9.8, P < 0.0001). Of the participant who were overweight/obese at Wave-3, 86.2% continued to be overweight/obesity at Wave-4 (OR 22.5, P < 0.0001). Underweight status was also significantly stable throughout the follow-ups. Of the participants who were underweight at Wave-2, 76.7% were underweight at Wave-3 (OR 22.6, P < 0.0001) and 46.7% remained underweight at Wave-4 (OR 9.8, P < 0.0001). Of underweight participants at Wave-3, 83.8% were underweight at Wave-4 (OR 17.3, P < 0.0001).

There was significant tracking of both low and high WHtR in all follow-ups. Sex was a significant confounder in most analyses (table 3) with tracking of low WHtR being more likely for male participants and tracking of high WHtR more likely for female participants. Of the participants who had a low WHtR at Wave-2, 44.7% remained in the same category at Wave-3 (OR 6.9, P < 0.0001) and 23.7% at Wave-4 (OR 4.5, P=0.001) while 46.7% of participants with a low WHtR at Wave-3 having a low WHtR at Wave-4 (OR 45.1, P < 0.0001). Of the participants with a high WHtR at Wave-2, 71.1% had a high WHtR at Wave-3 (OR 9.3, P<0.0001) and 94.7% at Wave-4 (OR 28.6, P <0.0001). Of the participants with a high WHtR at Wave-3, 85.1% remained in the same category at Wave-4 (OR 11.3, P<0.0001). Peer

Sensitivity analyses

To test for bias due to the large amount of people not included, sensitivity analyses were performed for tracking analyses for all plausible values for the whole cohort. Logistic regression analyses adjusted for sex, age at follow-up and time between follow-ups determined that tracking of overweight/obesity was significant from Wave-2 to Wave-3 (P<0.0001, OR=17.3) and Wave-4 (P<0.0001, OR=16.1) as well as from Wave-3 to Wave-4 (P<0.0001, OR=18.7). Tracking was also significant for underweight from Wave-2 to Wave-3 (P<0.0001, OR=15.8) and to Wave-4 (P=0.003, OR=4.1) and from Wave-3 to Wave-4 (P<0.0001, OR=11.2). High WHtR tracked from Wave-2 to Wave-3 (P<0.0001, OR=9.9) and to Wave-4 (P<0.0001, OR=21.8) and from Wave-3 to Wave-4 (P<0.0001, OR=7.9). Low WHtR tracked from Wave-2 to Wave-3 (P=0.002, OR=2.6) and to Wave-4 (P=0.005, OR=2.4) and from Wave-3 to Wave-4 (P<0.0001, OR=7.8).

²Table 2. Associations between weight classes at different timepoints

4 5 6			Underweight	ce (Wave-3)	Ove	erweight/obese			Adulthood (Wave-4) Underweight Overweight/ob					
7 8 Childhood		%	OR (CI)		P-value	%	OR(CI)	P-value	%	OR (CI)	P-value	%	OR (CI)	P-value
9 Childhood 9 (Wave-2) 10	Underweight	76.7%	22.6 (12.2-42.0)		<0.0001	0%	-	-	46.7%	9.8 (5.2-18.6)	<0.0001	8.3%	0.09 (0.04-0.2)	<0.0001
11	Normal weight	17.7%	0.15 (0.09-0.3)		<0.0001	20.9%	1.4 (0.8-2.5)	0.25	10.8%	0.2 (0.1-0.4)	<0.0001	43.0%	2.1 (1.3-3.5)	0.002
12 13 Adolescence	Overweight/obese	0%	-		-	67.6%	16.0 (7.1-35.7)	<0.0001	2.7%	0.07 (0.009-0.5)	0.0095	83.8%	13.2 (5.3-33.0)	<0.0001
¹⁴ (Wave-3)	Underweight	-	-		-	-	-	-	83.8%	17.3 (8.5-35.2)	<0.0001	3.3%	0.03 (0.009-0.08)	<0.001
15 16	Normal weight	-	-		$\mathcal{O}_{\mathbf{a}}$	-	-	-	16.2%	0.2 (0.09-0.34)	<0.0001	40.2%	1.6 (0.98-2.5)	0.06
17 18	Overweight/obese	-	-		- 6	5.	-	-	0%	-	-	86.2%	22.5 (10.0-51.0)	<0.0001

Tracking of weight classes from childhood and adolescence to adolescence and adulthood, eg. of the children who were underweight at first follow-up, 76.7% remained underweight in adolescence and 46.7% in adulthood. 2 Weight classes for participants < 18 years of age based on age and sex specific BMI cut-off points according to Cole et al. (2000, 2007). For adults: underweight BMI < 18.5; normal weight BMI 18.5-24.99; overweight/obese BMI ≥ 25. 22 R adjusted for age (years) at earlier follow-up, time (years) between follow-ups and sex. % indicates percent of participants in weight class at later follow-up.

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Table 3. Associations between low and high WHtR at different time points

7																					
8		Adolescence (Wave-3)										Adulthood (Wave-4)									
9				WHtR < 0.4	4				WHtR≥0.5					WHtR < 0	.4				WHtR ≥ 0.5	5	
10						P-value					P-value					P-value					P-value
1 1 Childhood		%	OR (CI)	P-value	OR for sex	for sex	%	OR(CI)	P-value	OR for sex	for sex	%	OR (CI)	P-value	OR for sex	for sex	%	OR(CI)	P-value	OR for sex	for sex
																				(
(₩ <u>2</u> ave-2)	WHtR < 0.4	44.7	6.9 (3.2-15.1)	<0.0001	3.2 (1.6-6.4)	0.001	2.6	0.05 (0.007-0.4)	0.004	0.4 (0.3-0.7)	0.002	23.7	4.5 (1.8-11.4)	0.001	3.5 (1.5-8.6)	0.005	21.1	0.2 (0.1-0.5)	0.0005	0.4 (0.2-0.6)	<0.0001
13	WHtR ≥ 0.5	0.0	-	-	-	-	71.1	9.3 (4.2-20.4)	<0.0001	0.5 (0.3-0.8)	0.005	0.0	-	-	-	-	94.7	28.6 (6.6-122.9)	< 0.0001	0.4 (0.2-0.6)	<0.0001
A deplescence													26.7 (10.3-								
	WHtR < 0.4	-	-	-	-	-	-	- 6	-	-	-	45.1	69.2)	<0.0001	2.0 (0.8-5.3)	0.2	9.8	0.1 (0.04-0.3)	<0.0001	0.5 (0.3-0.7)	0.001
16	WHtR ≥ 0.5	-	-	-	-	-	-		-	-	-	0.0	-	-	-	-	85.1	11.3 (5.8-21.9)	<0.0001	0.5 (0.3-0.8)	0.003

1/ Fracking of waist-to-height ratio from childhood and adolescence to adolescence and adulthood. OR adjusted for age (years) at earlier follow-up, time (years) between follow-ups and sex. OR for sex modeled as male (years) female. % indicates per cent of participants in WHtR at later follow-up.

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DISCUSSION

In this Indigenous cohort, underweight was common from childhood through to adolescence and young adulthood. Overweight/obesity was relatively less common but increased across time. This is in contrast to the general Australian Indigenous population, where rates of overweight and obesity are higher. It may reflect the cohort demographics with many people residing in remote and very remote communities.

There is significant tracking of nutritional status from childhood to adulthood among Indigenous Australians in this cohort, both when assessed with BMI or WHtR categories. In contrast to BMI, there were significant differences between the sexes for both tracking and prevalence of WHtR categories with females more often presenting with central adiposity in adolescence and adulthood. This finding is consistent with previous studies that show that Indigenous women in general have greater waist circumference than their non-Indigenous counterparts.[30-31] We have previously reported that females in this cohort have lower levels of physical activity, which may be a possible contributing factor.[32] Central adiposity is a known risk factor for cardiovascular morbidity which accounts for a substantial part of the disparity in health outcomes between Indigenous and non-Indigenous Australians. Therefore, women seem to be at particular risk for chronic disease due to their body fat composition.[31]

Both areal disadvantage and remote residence were associated with lower prevalence of overweight/obesity and higher rates of underweight. This is in contrast to a study from New South Wales that examined Indigenous people aged 45 and older, where participants from more advantaged and urban surroundings had lower prevalences of obesity and overweight than those from remote and disadvantaged areas [16]. In a previous study from the ABC, a significant association was found between remoteness and areal disadvantage at birth and longitudinal development of BMI measured at the same follow-ups as the present study. [33] It seems that the

spatial trend in obesity in this cohort is similar to that traditionally seen in low and middle income countries, where obesity is more concentrated in cities and wealthier regions and underweight is more common in remote and rural settings. [1] The dual burden of malnutrition and the urban-remote differential in nutritional status has been previously described in the cohort at an average age of 25 years.[34]

The association between maternal BMI and offspring BMI is consistent with previous studies conducted in non-Indigenous cohorts. In the Generation R study, it was found that maternal obesity is associated with adverse cardiometabolic risk profiles including obesity, higher systolic blood pressure and adverse lipid levels in the offspring at the age of six years.[35] In the Avon Longitudinal Study of Parents and Children (ALSPAC), a linear trend between maternal prepregnancy BMI and offspring adiposity levels was found: offspring of underweight mothers had lower rates and offspring of overweight mothers had higher rates of adiposity at 7.5 and 17.2 years. DNA methylation was suggested as a mediating factor.[36]

From a public health point of view, the present paper presents further evidence that dietary interventions need more tailored approaches, as there exist large variations within the Indigenous communities regarding nutritional status and its behaviour over time. Interventions need to be delivered within critical time windows and the gender perspective is essential: pre-pregnant women and girls in general should receive special attention. [37] The reasons behind the dual burden of malnutrition, particularly the high rates of underweight in the remote and more disadvantaged communities, are multifactorial and include high food prices, low incomes, overcrowded households and rudimentary cooking facilities [38-39]. Approaches that have been suggested to improve diet in the remote communities include eliminating socioeconomic constraints by reducing prices on fruit and vegetables in the community stores and enhancing nutrition-related consumer education and thus improving food security and self-efficacy to cook. [40] Nutrition education including cooking skills workshops, group education sessions and store interventions have been

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reported to have some positive effect on obesity in Indigenous communities according to a review study that included both remote and urban communities in Australia [41]. Multi-sector participatory approaches to strengthen food systems in remote Indigenous communities are needed [42] with a special focus on nutrition in the early life.

The strengths of the study include its longitudinal design and well-structured follow-ups with relatively good retention rates. The study population however is relatively small causing some limitations to the interpretation of the results and as only participants with data from all follow-ups were included, the missing data was quite substantial. However, the results from the sensitivity analyses where all data points were analysed were similar to the analyses presented. There were significant geographical differences between participants and non-participants, with participants being more often from non-urban and more disadvantaged areas. This potential bias may exaggerate the prevalences for underweight in the cohort as underweight was more prevalent in the remote and disadvantaged regions. The presented associations between weight status and socioeconomic status, remoteness, maternal BMI and birth weight are merely descriptive analyses presented separately for each follow-up as the data was not analysed in a longitudinal fashion and correlation over time was not assessed as this was not the main aim of the article. Other limitations include the definition of socioeconomic status, as the individual level indicators of socioeconomic status such as income were not available. IRSEO describes socioeconomic disadvantage on an area level and may not reflect the individual situation of the participants. Finally, the participants were still young during the last follow-up. After future follow-ups, cardiovascular morbidity and clinical events are likely to be more prevalent and could be analysed for even better understanding of the clinical relevance of the nutritional status and obesity trends in this cohort.

In summary, this study presents strong evidence on tracking of nutritional status from childhood to adulthood in this unique Indigenous cohort. Socioeconomic status and remoteness factors were associated with weight status in all follow-ups. The high prevalence of underweight across all age

> groups requires special attention in the process of improving nutritional health in the remote Indigenous communities. The differences in central adiposity between males and females that seem to arise after childhood indicate a need for targeted and successfully timed approaches in dietary interventions.

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FIGURE LEGENDS

Figure 1. Percentages of underweight and overweight/obese participants by sex. For classification, age and sex specific cut-off points were used for participants under 18 years of age at follow-up. For participants aged 18 and over, underweight was classified as BMI < 18,5; normal weight as 18,5-24,99; overweight as 25-29,99 and obesity as \geq 30.

Figure 2. Prevalences for low and high waist-to-height ratio at three time points according to sex. P-values are calculated with chi-square tests and represent differences between sexes. Values are in percentages.

Figure 3. Prevalences of overweight/obesity and underweight in participants according to urban residence (A), maternal BMI (B), areal disadvantage (C), and birth weight (D). Chi-square tests were used to assess association between weight status and presented categories.

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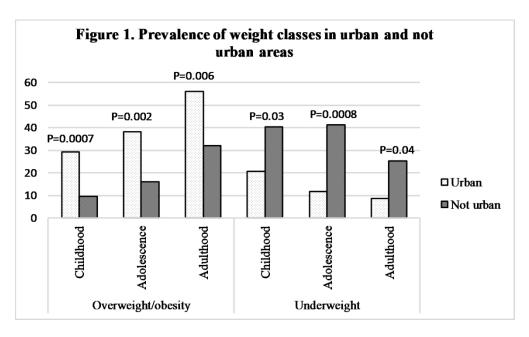
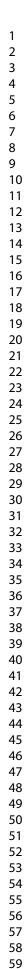


Figure 1. Percentages of underweight and overweight/obese participants by sex. For classification, age and sex specific cut-off points were used for participants under 18 years of age at follow-up. For participants aged 18 and over, underweight was classified as BMI < 18,5; normal weight as 18,5-24,99; overweight as 25-29,99 and obesity as ≥ 30 .

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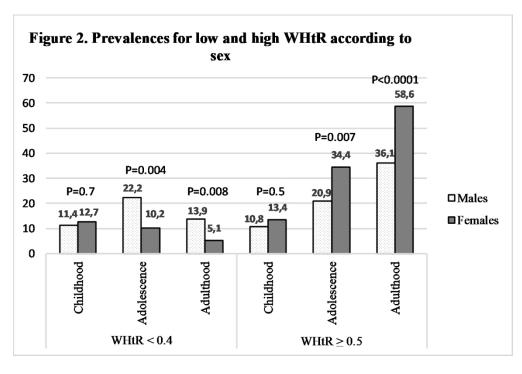


Figure 2. Prevalences for low and high waist-to-height ratio at three time points according to sex. P-values are calculated with chi-square tests and represent differences between sexes. Values are in percentages.

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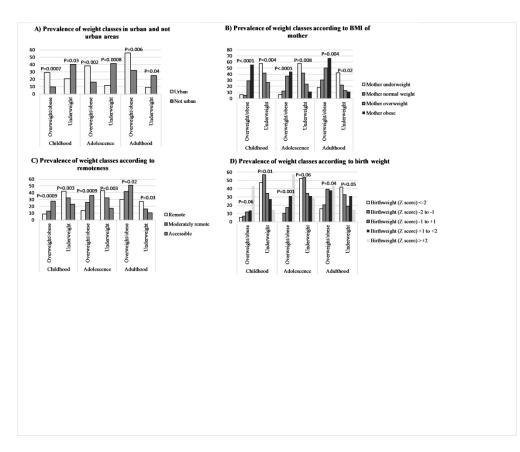


Figure 3. Prevalences of overweight/obesity and underweight in participants according to urban residence (A), maternal BMI (B), areal disadvantage (C), and birth weight (D). Chi-square tests were used to assess association between weight status and presented categories.

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	Participants (N=315)	Dropouts (N=371)	P-value
Males (%)	50.2	53.1	P=0.44
Urban residence (%)	10.8	31.8	P<0.0001
Birthweight, z score	-0.29	-0.30	P=0.95
IRSEO score	80.8	65.9	P<0.0001
Maternal BMI	22.2	22.3	P=0.71

Comparison between participants and dropouts. Values for categorical variables (sex, urban residence) are presented in percentages and values for continuous variables in means. Chisquare tests were used for analysis of categorical variables and t-tests for continuous variables.

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STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	2
		(<i>b</i>) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			1
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(<i>a</i>) Give the eligibility criteria, and the sources and methods of selection of	5
	-	participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	6-7
		effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	6-7
measurement		assessment (measurement). Describe comparability of assessment methods if	
D.	0	there is more than one group	5, 1
Bias	9	Describe any efforts to address potential sources of bias	5
Study size Quantitative variables	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(<i>a</i>) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, explain how loss to follow-up was addressed	
		(<u>e</u>) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially	5
		eligible, examined for eligibility, confirmed eligible, included in the study,	
		completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	tabl
		and information on exposures and potential confounders	1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	tabl

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16	(a) Cive up adjusted estimates and if applicable confounder adjusted estimates and their	8-10
16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their	
	(b) Report category boundaries when continuous variables were categorized	
	(c) If relevant, consider translating estimates of relative risk into absolute risk for a	
	meaningful time period	
17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity	
	analyses	
18	Summarise key results with reference to study objectives	10- 11
19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.	12
	Discuss both direction and magnitude of any potential bias	
20	Give a cautious overall interpretation of results considering objectives, limitations,	11-
	multiplicity of analyses, results from similar studies, and other relevant evidence	12
21	Discuss the generalisability (external validity) of the study results	12
on		
	17 18 19 20 21	 precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period 17 Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses 18 Summarise key results with reference to study objectives 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence 21 Discuss the generalisability (external validity) of the study results

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

applicable, for the original study on which the present article is based

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Socioeconomic status, remoteness, and tracking of nutritional status from childhood to adulthood in an Australian Aboriginal Birth Cohort - the ABC study.

Journal:	BMJ Open
Manuscript ID	bmjopen-2019-033631.R2
Article Type:	Research
Date Submitted by the Author:	08-Jan-2020
Complete List of Authors:	Sjöholm, Pauline; University of Turku, Department of Medicine; Vaasa Central Hospital Pahkala, Katja; University of Turku, Research Centre of Applied and Preventive Cardiovascular Medicine; University of Turku, Paavo Nurmi Centre, Sports & Exercise Medicine Unit, Department of Physical Activity and Health Davison, Belinda; Menzies School of Health Research Juonala, Markus; University of Turku, Department of Medicine; Murdoch Childrens Research Institute Singh, Gurmeet; Menzies School of Health Research; Flinders University, Northern Territory Medical Program
Primary Subject Heading :	Nutrition and metabolism
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	SOCIAL MEDICINE, PUBLIC HEALTH, Community child health < PAEDIATRICS, NUTRITION & DIETETICS, EPIDEMIOLOGY

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Socioeconomic status, remoteness, and tracking of nutritional status from childhood to adulthood in an Australian Aboriginal Birth Cohort – the ABC study.

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This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Conflicts of interest: The authors report no relationships that could be construed as a conflict of interest.

Contributorship statement: P.S., K.P., B.D., G.S. and M.J. contributed to the analysis and interpretation of data. B.D. and G.S. were responsible for the design and implementation of the larger study of which this paper is a part. B.D and G.S. collected and managed the data used in this study. P.S. wrote the paper with input from all authors. All authors approved of the final version to be submitted and agree to be accountable for all aspects of the work.

Funding: The authors received no specific funding for this paper

Data sharing statement: All data are stored confidentially and are not freely available in the public domain, but specific proposals for collaboration are welcomed. Collaborations are established through formal agreement with the ABC steering committee. Contact information: abcstudy@menzies.edu.au

Ethics statement: This study was approved by the Human Research Ethics Committee of Northern Territory Department of Health and Menzies School of Health Research, including the Aboriginal Ethical Sub-committee which has the power of veto (ABC Reference no. 2013-2022). All research was performed in accordance with the National Health and Medical Research Council guidelines (National Statement on Ethical Conduct in Human Research, 2008). Informed written consent was obtained from all participants.

Key words: Nutritional Status, Indigenous, Socioeconomic

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ABSTRACT

Objectives: To determine prevalences of underweight and overweight as well as low and high waist-to-height ratio (WHtR) in three prospective follow-ups and to explore tracking of these measures of nutritional status from childhood to adolescence and adulthood. The influence of socioeconomic status, remoteness, maternal body mass index (BMI) and birth weight on weight status was assessed.

Design: Longitudinal birth cohort study of Indigenous Australians.

Setting: Data derived from three follow-ups of the Aboriginal Birth Cohort (ABC) study with mean ages of 11.4, 18.2 and 25.4 years for the participants.

Participants: Of the 686 Indigenous babies recruited to the study between 1987-1990, 315 had anthropometric measurements for all three follow-ups and were included in this study.

Primary and secondary outcome measures: Categories for BMI (underweight, normal weight, overweight and obesity) and WHtR (low and high), sex, areal socioeconomic disadvantage as defined by the Indigenous Relative Socioeconomic Oucomes index, urban/remote residence, maternal BMI, birth weight. Logistic regression was used to calculate odds ratios for belonging to a certain BMI category in adolescence and adulthood according to BMI category in childhood and adolescence.

Results: Underweight was common (38% in childhood and 24% in adulthood) and the prevalence of overweight/obesity increased with age (12% in childhood and 35% in adulthood). Both extremes of weight status as well as low and high WHtR tracked from childhood to adulthood. Underweight was more common and overweight less common in remote and more disadvantaged areas. Birth weight and maternal BMI were associated with later weight status. There were significant sex differences for prevalences and tracking of WHtR but not for BMI.

Conclusions: Socioeconomic factors, remoteness and gender must be addressed when assessing nutrition-related issues in the Indigenous communities due to the variation in nutritional status and its behaviour over time within the Indigenous population.

ARTICLE SUMMARY

Strengths and limitations of this study

- This cohort is the longest-running and largest Indigenous birth cohort in Australasia and presents unique data about the health of the contemporary Indigenous population.
- Despite logistic challenges relating to geography and accessibility, the retention rates were good.
- The present study offers novel findings about the geographical, socioeconomic and gender differences in nutritional status that should be addressed when developing new strategies to reduce the immense health inequalities in Australia.
- The study population was relatively small with a substantial amount of missing data.
- At this young age, the participants are healthy with very few showing overt disease, thus analysis of morbidity was not done. This will be addressed in future follow-ups.

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INTRODUCTION

The dual burden of malnutrition defined as the coexistence of obesity and underweight within individuals, households or populations is a phenomenon commonly seen in low and middle-income countries but less so in high-income countries.[1]

The Indigenous (used respectfully to include both Aboriginal and Torres Strait Islander peoples) population in Australia has experienced a dramatic nutritional transition since European colonisation.[2] Indigenous Australians, especially those living in remote regions, are prone to a number of morbidities associated with non-favourable nutrition throughout life.[3] In 2012-2013, Indigenous Australians were 1.5 times as likely to be affected by obesity as non-Indigenous Australians, with 30% of Indigenous children aged 2-14 years and 66% of persons aged 15 and over being affected by overweight or obesity.[4] However, underweight was almost twice as common in childhood: 8% of Indigenous children were underweight compared with 4.8% of non-Indigenous children.[5] Obesity is a well documented risk factor for cardiovascular disease, type 2 diabetes, cancer and several other non-communicable diseases [6-7] while underweight, a possible manifestation of malnutrition and nutritional deficiencies,[8] is also associated with raised infection risk[9] and pregnancy complications.[10] Both extremes of body composition are associated with substantial medical costs for the communities involved.[11] Overweight and obesity tend to 'track' from childhood to adulthood, i.e. remain relatively stable throughout an individual's lifecourse, according to studies conducted in non-Indigenous populations.[12] Tracking of underweight is a topic less studied, but has been reported in some cohorts.[13] There is a paucity of data in Indigenous children and adolescents regarding tracking of nutritional status.

In high-income countries, low socioeconomic status has been shown to be associated with obesity.[14] However, in low and middle income countries, the association is often reversed, and persons of higher socioeconomic status are more likely to be affected by obesity.[15] The effects of socioeconomic factors and remoteness on nutritional status have generally been similar for the Indigenous and the non-Indigenous Australians with obesity being concentrated in urban and less disadvantaged areas. [4, 16] To our knowledge, there have been no studies examining the longitudinal development of nutritional status and its associations with socioeconomic factors in very remote regions of Australia, where food insecurity is high [17] and malnutrition and underweight are more common [18].

The Aboriginal Birth Cohort (ABC) was formed to better understand the reasons behind the high burden of disease of the Australian Indigenous population and identify possibilities for early prevention. To date, the study is one of the longest running and largest Indigenous birth cohorts in Australasia. The intention of this paper is 1) to explore tracking of nutritional status from childhood to adulthood and 2) to explore the association of socioeconomic status and remoteness at birth with later nutritional status in the cohort.

METHODS

Participants

Details of the recruitment and follow-up of the ABC have been previously published in detail.[19-20] In brief, between 1987 and 1990, 686 of the eligible 1238 babies born to Indigenous mothers at the Royal Darwin Hospital were recruited into the study. There were no differences for mean birth weights or sex ratios between those recruited and those not recruited. Since recruitment (Wave-1), three follow-ups have been conducted: in childhood (Wave-2) at a mean age of 11.4 years (n=572; 86 % of living participants), in adolescence (Wave-3) at a mean age of 18.2 years (n=469; 71 % of

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living participants) and most recently in early adulthood (Wave-4) at a mean age of 25.4 years (n=459; 71 % of living participants).

All procedures contributing to this work comply with the Helsinki Declaration of 1975, as revised in 2008. All participants provided written informed consent to participate in this study, and all procedures were approved by the Human Research Ethics Committee of the Northern Territory Department of Health and the Menzies School of Health Research, including the Aboriginal Ethical Sub-committee which has the power of veto.

Patient and public involvement

The study has clear commitment to engaging with Indigenous communities and building Indigenous capacity. Indigenous researchers have been involved in all aspects of the study at each of the follow-ups including investigators, data collection team and local community members employed as research assistants, encouraging and facilitating formal research training. Extensive consultation with expert, Indigenous and cohort reference groups was conducted prior to each follow-up to obtain advice and guidance on contact methods, acceptability of planned procedures and methods of feedback to individuals and communities. Due to the difficulty in providing individual feedback after the initial visit, feedback is aimed at the community level in remote areas. Updates are published in community newsletters and in the national Aboriginal and Islander Health Worker Journal and provided to local community groups, stakeholders and governance groups.

Anthropometric measurements

At birth, maternal height and weight was recorded and used to calculate body mass index (BMI; kg/m²) which was classified as underweight (< 18.5), normal weight (18.5-24.99), overweight (25-29.99) or obese (\geq 30). Birthweight of the participants was transformed into Z-scores and put into 5

categories based on the WHO child growth charts [21] 1) low: <-2; 2) low-normal: -2 to -1; 3) normal: -1 to 1; 4) normal-high: 1 to 2; and 5) high >2.

At each follow-up of the study, a small group (3-4) of trained researchers measured height and weight using standardized methods. Weight was measured in light clothing while barefoot to the last complete 0.1 kg with a digital scale (TBF-521; Tanita Corporation, Arlington Heights, Illinois, USA). Height was measured with a portable stadiometer to the nearest millimeter. BMI was calculated as weight (kg) divided by height (m) squared. Waist circumference was measured to the nearest millimeter using a flexible tape measure at the midpoint between the lowest rib and iliac crest at the end of exhalation.

Participants were categorised in classes of nutritional status using two alternative classifications: Body mass index (BMI), a widely used estimate for defining weight status and waist-to-height ratio (WHtR), an alternative anthropometric measure to define adiposity.

For participants who had attained 18 years at follow-up, the following BMI categories were used: underweight <18,5, normal weight 18.5-24.99, overweight 25-29.99, obese \geq 30. For participants who were under 18 years of age at time of follow-up, age and sex specific cut-off points were used for categories of weight status (underweight, normal weight, overweight and obese) as defined by the International Obesity Task Force.[22-23]

WHtR has been suggested as a tool for better identifying abdominal obesity and delineating risk for cardiovascular disease and type 2 diabetes.[24] A cut-off value of 0.5 for WHtR has been commonly used for screening for cardio-metabolic risk irrespective of age, gender and ethnicity.[25–27] There is no consensus on a lower normal limit for WHtR, but a value of less than 0.4 has also been previously used. WHtR was calculated as waist circumference in centimeters divided by height in centimeters and categorised as low (<0.4), normal (0.4-0.49) or high $(\geq 0.5).[28]$

Remoteness and childhood socioeconomic situation

For areal socioeconomic disadvantage, the Indigenous Relative Socioeconomic Outcomes (IRSEO) index was used. The IRSEO is calculated at the Indigenous Area level and is based on 9 variables, 3 related to employment, 3 to education, 2 to housing and 1 to income, using information from the 2011 Census of Population and Housing. Each area is assigned to one of 100 percentiles, 1 for the most advantaged and 100 for the most disadvantaged. [29] Based on their reported addresses at birth, the participants were assigned an IRSEO score. The scores were categorised into three groups: low disadvantage (1 to 40), mid-high disadvantage (range 41 to 90), and high disadvantage (range 91 to 100).

Area of residence was classified at birth, with families residing in a rural community with an Aboriginal council classified as "remote" and all "non-remote" locations were classified as "urban". At Wave-4, 18 % of participants reported to have lived in another community at some point in their lives. However, limited movement between urban and remote settings was seen, with 8.7 % of participants who had lived in a remote community at birth moving to an urban community by Wave-4 and 19 % of the participants who had lived in an urban community at Wave-2 moving to a remote location at by Wave-4.

Statistical analyses

Participants who were pregnant at Wave-3 and/or Wave-4 were excluded from the analyses. Only participants who had height, weight and waist circumference recorded at all follow-ups were included (N=315). Overweight and obesity were combined into one category due to small numbers. Attrition analyses were performed to compare baseline characteristics between participants included and not included at each follow-up with t-tests for continuous and chi-square tests for categorical

variables. Chi-square tests were used to assess the association of weight status and categories of remoteness, socioeconomic status, maternal BMI and birth weight at all follow-ups separately. Tracking of nutritional status (underweight, overweight/obese and WHtR, low and high) was analysed using logistic regression and reported as odds ratio (OR) of status being constant across time: status in childhood continuing into adolescence and adulthood and status in adolescence continuing into adulthood. Regression analyses were adjusted for age at follow-up, sex and time between compared follow-ups as well as IRSEO category that was used as a proxy for socioeconomic status.

To assess the changes over time, Cochran's Q tests and McNemar's tests were used to analyse the differences in the proportions of nutritional status categories by sex over the course of the three follow-ups.

Statistical tests were performed with SAS version 9.4 (SAS Institute, Inc, Cary, NC). Statistical significance was inferred at a 2-tailed P-value < 0.05.

Results

Complete data (height, weight and waist circumference) at all follow-ups were available on 315 participants. There were no significant differences in sex, birth weight and maternal BMI in participants included and those not included. There were significant differences between the two groups regarding remoteness and areal disadvantage: those included were more often from remote and more disadvantaged areas according to IRSEO scores (see supplementary table 1). There were no significant differences between the BMI or the WHtR values at any follow-up between participants included and those not included (for BMI: P=0.48 for wave-2 and 3, P=0.47 for wave-4; for WHtR P=0.5, 0.46 and 0.52 respectively). Descriptive statistics of the participants are presented in table 1.

Anthropometric characteristics of participants

	Childhood	l (Wave-2)	Adolescenc	e (Wave-3)	Adulthoo	d (Wave-4)
	Male	Female	Male	Female	Male	Female
Age, years ± SD	11.1 ± 1.1	10.8 ± 1.1	17.9 ± 1.1	17.7 ± 1.1	25.4 ± 1.1	25.2 ± 1.2
Weight, kg	34.3 ± 11.5	35.2 ± 11.5	64.1 ± 20.2	53.7 ± 13.0	71.1 ± 21.2	60.6 ± 16.0
Height, cm	143.1 ± 10.1	143.0 ± 10.5	173.3 ± 6.9	161.3 ± 5.2	174.3 ± 7.0	161.4 ± 5.6
BMI	16.4 ± 3.5	16.8 ± 3.4	21.2 ± 5.6	20.7 ± 4.9	23.3 ± 6.0	23.3 ± 6.2
Waist circumference, cm	63.8 ± 9.5	63.9 ± 9.0	78.8 ± 14.5	77.7 ± 12.6	85.7 ± 16.0	86.2 ± 15.1
WHtR	0.45 ± 0.05	0.45 ± 0.05	0.45 ± 0.08	0.48 ± 0.08	0.49 ± 0.09	0.54 ± 0.1

Birth characteristics of participants

	Male	Female	Total
N	158 (50.2%)	157 (40.8%)	315
Urban residence, %	13.3	8.3	10.8 (N=315)
Birth weight, Z score ± SD	-0.16 ± 1.2	-0.42 ± 1.1	-0.29 ± 1.1 (N=293)
IRSEO score	78.6 ± 23.9	83.0 ± 19.7	80.8 ± 22.0 (N=315)
BMI of mother	22.0 ± 3.8	22.6 ± 4.4	22.3 ± 4.1 (N=236)

Table 1. Descriptive characteristics. Mean values with standard deviations for anthropometric measurements of participants in three follow-ups and baseline characteristics.

High rates of underweight were seen at all 3 follow-ups: 38.1 % at Wave-2, 38.1 % at Wave-3 and 23.5 % at Wave-4. Overweight and obesity increased over time: for overweight, 8.9 % at Wave-2, 12.1% at Wave-3 and 22.9 % at Wave-4, and for obesity, 2.9 %, 6.4 % and 11.8 % respectively. Prevalences of BMI categories according to sex are presented in figure 1. There were no significant differences between the sexes in the prevalence of underweight, overweight or obesity.

The differences in weight status over the course of the three follow-ups were significant with rates of underweight decreasing and rates of overweight/obesity rising (P<0.0001 for underweight and overweight/obesity for both sexes). There was no statistically significant difference in the rate of underweight between Wave-2 and Wave-3 (P=0.56 for males and P=0.76 for females) but a significant difference in the prevalence of underweight between Wave-2 and Wave-4 (P<0.0001 for both sexes). For the prevalences of overweight/obesity, there was a statistically significant difference between Wave-2 and Wave-3 for male participants but not for females (P=0.002 for males and P=0.16 for females). Between

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Wave-2 and Wave-4 the difference was statistically significant for both sexes (P<0.0001) as well as between Wave-3 and Wave-4 (P=0.0007 for males and P<0.0001 for females).

Prevalences of low (<0.4) and high (\geq 0.5) WHtR in the three follow-ups are presented in figure 2. There were no differences between the sexes at Wave-2. In later follow-ups, male participants more often had a low WHtR (22.2 vs. 10.2 % at Wave-3 [P=0.004] and 13.9 vs. 5.1 % at Wave-4 [P=0.008]) while female participants more often had a high WHtR (34.4 vs. 20.9 % at Wave-3 [P=0.007] and 58.6 vs. 36.1 % at Wave-4 [P<0.0001]). The changes in WHtR over the course of the three follow-ups were significant with rates of low WHtR decreasing and rates of high WHtR rising (P=0.002 for males and P=0.03 for females for low WHtR and P<0.0001 for both sexes for high WHtR). Between Wave-2 and Wave-3, there was a statistically significant difference between the rates for low WHtR for males (P=0.003) but not for females (P=0.4). Between Wave-2 and Wave-4 the difference was significant between Wave-2 and Wave-3 (P=0.002 for males and P<0.0001 for females (P=0.01) but not for males (P=0.4). For high WHtR, the difference was significant between Wave-2 and Wave-3 (P=0.002 for males and P<0.0001 for females (P=0.01) but not for males and P<0.0001 for high WHtR, the difference was significant between Wave-2 and Wave-3 (P=0.002 for males and P<0.0001 for females) and between Wave-2 and Wave-4 (P<0.0001 for both sexes).

The associations between weight class and remoteness, maternal BMI, areal disadvantage (IRSEO) and birth weight are presented in figure 3. Urban participants were significantly more likely to be overweight/obese and less likely to be underweight than remote participants in all follow-ups. Areal socioeconomic disadvantage was significantly associated with weight class in all follow-ups: participants from more disadvantaged areas were more often underweight and less often overweight/obese than participants from less disadvantaged areas. Maternal weight status was significantly associated with offspring weight status in all follow-ups with children of underweight mothers being more often underweight and children of overweight and obese mothers more often presenting with overweight and obesity. Birth weight was also associated with later weight status: smaller babies were more often underweight and less often overweight or obese in all follow-ups.

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The association was significant in all follow-ups except for overweight status at Wave-2 (P=0.06) and underweight status at Wave-3 (P=0.06).

Analyses of tracking of weight status according to BMI categories are presented in table 2. Tracking was significant between age groups for all BMI categories, with sex not a significant confounder in any of the analyses. Of the participants who were overweight/obese at Wave-2, 67.6% remained in the same weight status category at Wave-3 (OR 12.9, P < 0.0001) and 83.8% at Wave-4 (OR 10.9, P < 0.0001). Of the participants who were overweight/obese at Wave-3, 86.2% continued to be overweight/obese at Wave-4 (OR 21.3, P < 0.0001). Conversely, of the participants who were overweight/obese already at Wave-2 and 45.9% at Wave-3. Underweight status also showed significant tracking throughout the follow-ups. Of the participants who were underweight at Wave-2, 76.7% were underweight at Wave-3 (OR 22.6, P < 0.0001) and 46.7% remained underweight at Wave-4 (OR 9.8, P < 0.0001). Of underweight participants at Wave-3, 83.8% were underweight at Wave-4 (OR 17.3, P < 0.0001).

There was significant tracking of both low and high WHtR in all follow-ups. Sex was a significant confounder in most analyses (table 3) with tracking of low WHtR being more likely for male participants and tracking of high WHtR more likely for female participants. Of the participants who had a low WHtR at Wave-2, 44.7% remained in the same category at Wave-3 (OR 8.5, P < 0.0001) and 23.7% at Wave-4 (OR 4.7, P=0.003) while 45.1% of participants with a low WHtR at Wave-3 had a low WHtR at Wave-4 (OR 21.3, P < 0.0001). Of the participants with a wave-3 had a low WHtR at Wave-4 (OR 21.3, P < 0.0001). Of the participants with a high WHtR at Wave-2, 71.1% had a high WHtR at Wave-3 (OR 8.3, P<0.0001) and 94.7% at Wave-4 (OR 25.0, P <0.0001). Of the participants with a high WHtR at Wave-3, 85.1% remained in the same category at Wave-4 (OR 10.3, P<0.0001). Of the participants who had a high WHtR in adulthood, 24.2% had a high WHtR already in childhood and 49.7% in adolescence.

Sensitivity analyses

To test for bias due to the large amount of dropouts, sensitivity analyses were performed for tracking analyses for all plausible values for the whole cohort. Logistic regression analyses adjusted for sex, age at follow-up and time between follow-ups determined that tracking of overweight/obesity was significant from Wave-2 to Wave-3 (P<0.0001, OR=17.3) and Wave-4 (P<0.0001, OR=16.1) as well as from Wave-3 to Wave-4 (P<0.0001, OR=18.7). Tracking was also significant for underweight from Wave-2 to Wave-3 (P<0.0001, OR=15.8) and to Wave-4 (P=0.003, OR=4.1) and from Wave-3 to Wave-4 (P<0.0001, OR=11.2). High WHtR tracked from Wave-2 to Wave-3 (P<0.0001, OR=21.8) and from Wave-3 to Wave-4 (P<0.0001, OR=21.8).

² Table 2. Associations between weight classes at different timepoints

	Adolescence (Wave-3) Underweight			Overweight/obese			Adulthood (Wave- Underweight			-4) Overweight/obese		
	%	OR (CI)	P-value	%	OR(CI)	P-value	%	OR (CI)	P-value	%	OR (CI)	P-value
Underweight	76.7%	20.5 (10.9-38.7)	<0.0001ŧ	0%	-	-	46.7%	8.8 (4.6-17.0)	<0.0001ŧ	8.3%	0.09 (0.04-0.2)	<0.0001
Normal weight	17.7%	0.15 (0.09-0.3)	<0.0001ŧ	20.9%	1.3 (0.7-2.5)	0.36ŧ	10.8%	0.2 (0.1-0.4)	<0.0001ŧ	43.0%	2.1 (1.3-3.5)	0.004ŧ
Overweight/obese	0%	- ^0	-	67.6%	12.9 (5.7-29.4)	<0.0001ŧ	2.7%	0.09 (0.01-0.7)	0.0095 †	83.8%	10.9 (4.3-27.8)	<0.0001ŧ
Underweight	-		· · .	-	-	-	83.8%	15.9 (7.6-32.9)	<0.0001	3.3%	0.03 (0.01-0.08)	<0.0001
Normal weight	-	-		-	-	-	16.2%	0.2 (0.09-0.3)	<0.0001ŧ	40.2%	1.4 (0.9-2.4)	0.06
Overweight/obese	-	-		5,	-	-	0%	-	-	86.2%	21.3 (9.1-49.9)	<0.0001
	Normal weight Overweight/obese Underweight Normal weight	Underweight76.7%Normal weight17.7%Overweight/obese0%Underweight-Normal weight-	Vinderweight OR (CI) Vinderweight 76.7% 20.5 (10.9-38.7) Normal weight 17.7% 0.15 (0.09-0.3) Overweight/obese 0% - Underweight - - Normal weight - -	% OR (Cl) P-value Underweight 76.7% 20.5 (10.9-38.7) <0.0001‡	Underweight P-value % % OR (Cl) P-value % Underweight 76.7% 20.5 (10.9-38.7) <0.0001 [‡] 0% Normal weight 17.7% 0.15 (0.09-0.3) <0.0001 [‡] 20.9% Overweight/obese 0% - - 67.6% Underweight - - - - Normal weight - - - -	Underweight Overweight/obese % OR (Cl) P-value % OR(Cl) Underweight 76.7% 20.5 (10.9-38.7) <0.0001 [‡] 0% - Normal weight 17.7% 0.15 (0.09-0.3) <0.0001 [‡] 20.9% 1.3 (0.7-2.5) Overweight/obese 0% - - 67.6% 12.9 (5.7-29.4) Underweight - - - - - - Normal weight - - - - - - Normal weight - - - - - -	Underweight Overweight/obese % OR (Cl) P-value % OR(Cl) P-value Underweight 76.7% 20.5 (10.9-38.7) <0.0001 [‡] 0% - - Normal weight 17.7% 0.15 (0.09-0.3) <0.0001 [‡] 20.9% 1.3 (0.7-2.5) 0.36 [‡] Overweight/obese 0% - - - - - Underweight 0.9% - - - - - - Normal weight 0.9% - - - - - - - Normal weight - - - - - - -	Underweight OR (Cl) P-value % OR (Cl) P-value % OR (Cl) P-value % A Underweight 76.7% 20.5 (10.9-38.7) <0.0001‡	Underweight Overweight/obese P-value % OR(Cl) % OR(Image:	UnderweightOR (C)P-value Λ OR(C)P-value Λ OR (C)P-value Λ Underweight76.7%20.5 (10.9-38.7)<0.001 $\frac{1}{2}$ 0%46.7%8.8 (4.6-17.0)<0.001 $\frac{1}{2}$ 8.3%Normal weight17.7%0.15 (0.09-0.3)<0.001 $\frac{1}{2}$ 20.9%1.3 (0.7-2.5)0.36 $\frac{1}{2}$ 10.8%0.2 (0.1-0.4)<0.001 $\frac{1}{2}$ 43.0%Overweight/obese0%67.6%12.9 (5.7-29.4)<0.001 $\frac{1}{2}$ 2.7%0.09 (0.01-0.7)0.0095 $\frac{1}{2}$ 83.8%Underweight16.2%0.2 (0.09-0.3)<0.001 $\frac{1}{2}$ 3.3%Normal weight16.2%0.2 (0.09-0.3)<0.001 $\frac{1}{2}$ 40.2%	Vinderweight Vinderweight P-value $\%$ OR(Cl) P-value $\%$ OR(Cl) $\%$ OR(Cl) $\%$ OR(Cl) $\%$ OR(Cl) $\%$ $\%$ OR(Cl) $\%$ <

Tracking of weight classes from childhood and adolescence to adolescence and adulthood, eg. of the children who were underweight at first follow-up, 76.7% remained underweight in adolescence and 46.7% in adulthood. 21 Weight classes for participants < 18 years of age based on age and sex specific BMI cut-off points according to Cole et al. (2000, 2007). For adults: underweight BMI < 18.5; normal weight BMI 18.5-24.99; overweight/obese BMI ≥ 2225. OR adjusted for age (years) at earlier follow-up, time (years) between follow-ups and sex. % indicates percent of participants in weight class at later follow-up. $\frac{1}{2}$ indicates that IRSEO category was a significant confounder.

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Table 3. Associations between low and high WHtR at different time points

Vave-4)
WHtR ≥ 0.5
P-value
OR(CI) P-value OR for sex for sex
1 0.2 (0.09-0.5) 0.0003 0.3 (0.2-0.5) <0.0001
7 25.0 (5.8-108.1) <0.0001 0.3 (0.2-0.6) <0.0001 [‡]
0.1 (0.04-0.3) <0.0001 0.5 (0.2-0.7) 0.0004
1 10.3 (5.3-20.1) <0.0001 0.4 (0.2-0.7) 0.001
1 7

Fracking of waist-to-height ratio from childhood and adolescence to adolescence and adulthood. OR adjusted for age (years) at earlier follow-up, time (years) between follow-ups and sex. OR for sex modeled as male so indicates per cent of participants in WHtR at later follow-up. $\frac{1}{2}$ indicates that IRSEO category was a significant confounder.

Calego, , .

DISCUSSION

In this Indigenous cohort, underweight was common from childhood through to adolescence and young adulthood. Overweight/obesity was relatively less common but increased across time. This is in contrast to the general Australian Indigenous population, where rates of overweight and obesity are higher. It may reflect the cohort demographics with many people residing in remote and very remote communities.

There is significant tracking of nutritional status from childhood to adulthood among Indigenous Australians in this cohort, both when assessed with BMI or WHtR categories. In contrast to BMI, there were significant differences between the sexes for both tracking and prevalence of WHtR categories with females more often presenting with central adiposity in adolescence and adulthood. This finding is consistent with previous studies that show that Indigenous women in general have greater waist circumference than their non-Indigenous counterparts. [30-31]

We have previously reported that females in this cohort have lower levels of physical activity, which may be a possible contributing factor.[32] Central adiposity is a known risk factor for cardiovascular morbidity which accounts for a substantial part of the disparity in health outcomes between Indigenous and non-Indigenous Australians. Therefore, women seem to be at particular risk for chronic disease due to their body fat composition.[31]

Both areal disadvantage and remote residence were associated with lower prevalence of overweight/obesity and higher rates of underweight. This is in contrast to a study from New South Wales that examined Indigenous people aged 45 and older, where participants from more advantaged and urban surroundings had lower prevalences of obesity and overweight than those from remote and disadvantaged areas [16]. In a previous study from the ABC, a significant association was found between remoteness and areal disadvantage at birth and longitudinal development of BMI measured at the same follow-ups as the present study. [33] It seems that the

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spatial trend in obesity in this cohort is similar to that traditionally seen in low and middle income countries, where obesity is more concentrated in cities and wealthier regions and underweight is more common in remote and rural settings. [1] The dual burden of malnutrition within the population and the urban-remote differential in nutritional status has been previously described in the cohort at an average age of 25 years.[34]

The association between maternal BMI and offspring BMI is consistent with previous studies conducted in non-Indigenous cohorts. In the Generation R study, it was found that maternal obesity is associated with adverse cardiometabolic risk profiles including obesity, higher systolic blood pressure and adverse lipid levels in the offspring at the age of six years.[35] In the Avon Longitudinal Study of Parents and Children (ALSPAC), a linear trend between maternal prepregnancy BMI and offspring adiposity levels was found: offspring of underweight mothers had lower rates and offspring of overweight mothers had higher rates of adiposity at 7.5 and 17.2 years. DNA methylation was suggested as a mediating factor.[36]

From a public health point of view, the present paper presents further evidence that dietary interventions need more tailored approaches, as there exist large variations within the Indigenous communities regarding nutritional status and its behaviour over time. Interventions need to be delivered within critical time windows and the gender perspective is essential: pre-pregnant women and girls in general should receive special attention.[37] The reasons behind the dual burden of malnutrition, particularly the high rates of underweight in the remote and more disadvantaged communities, are multifactorial and include high food prices, low incomes, overcrowded households and rudimentary cooking facilities [38-39]. Approaches that have been suggested to improve diet in the remote communities include eliminating socioeconomic constraints by reducing prices on fruits and vegetables in the community stores and enhancing nutrition-related consumer education and thus improving food security and self-efficacy to cook. [40] Nutrition education including cooking skills workshops, group education sessions and store interventions have been

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reported to have some positive effect on obesity in Indigenous communities according to a review study that included both remote and urban communities in Australia [41]. Multi-sector participatory approaches to strengthen food systems in remote Indigenous communities are needed [42] with a special focus on nutrition in the early life.

The strengths of the study include its longitudinal design and well-structured follow-ups with relatively good retention rates. The study population however is relatively small causing some limitations to the interpretation of the results and as only participants with data from all follow-ups were included, the missing data was quite substantial. However, the results from the sensitivity analyses where all data points were analysed were similar to the analyses presented. There were significant geographical differences between participants and non-participants, with nonparticipants being more often from urban and less disadvantaged areas. This potential bias may exaggerate the prevalences for underweight in the cohort as underweight was more prevalent in the remote and disadvantaged regions. The presented associations between weight status and socioeconomic status, remoteness, maternal BMI and birth weight are merely descriptive analyses presented separately for each follow-up as the data was not analysed in a longitudinal fashion and correlation over time was not assessed as this was not the main aim of the article. Other limitations include the definition of socioeconomic status, as the individual level indicators of socioeconomic status such as income were not available. IRSEO describes socioeconomic disadvantage on an area level and may not reflect the individual situation of the participants. Finally, the participants were still young during the last follow-up. After future follow-ups, cardiovascular morbidity and clinical events are likely to be more prevalent and could be analysed for even better understanding of the clinical relevance of the nutritional status and obesity trends in this cohort.

In summary, this study presents strong evidence on tracking of nutritional status from childhood to adulthood in this unique Indigenous cohort. Socioeconomic status and remoteness factors were associated with weight status in all follow-ups. The differences in central adiposity between males

> and females that seem to arise after childhood indicate a need for targeted and successfully timed approaches in dietary interventions. The high prevalence of underweight across all age groups requires special attention in the process of improving nutritional health overall in the remote Indigenous communities.

<text>

FIGURE LEGENDS

Figure 1. Percentages of underweight and overweight/obese participants by sex. For classification, age and sex specific cut-off points were used for participants under 18 years of age at follow-up. For participants aged 18 and over, underweight was classified as BMI < 18,5; normal weight as 18,5-24,99; overweight as 25-29,99 and obesity as \geq 30.

Figure 2. Prevalences for low and high waist-to-height ratio at three time points according to sex. P-values were calculated with chi-square tests and represent differences between sexes. Values are in percentages.

Figure 3. Prevalences of overweight/obesity and underweight in participants according to urban residence (A), maternal BMI (B), areal disadvantage (C), and birth weight (D). Chi-square tests were used to assess association between weight status and presented categories.

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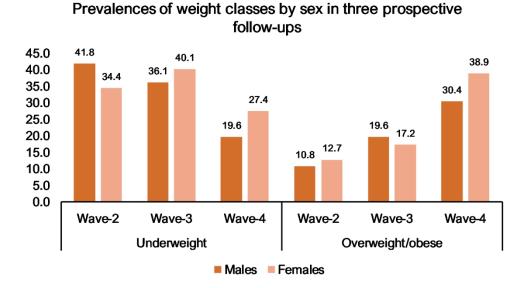
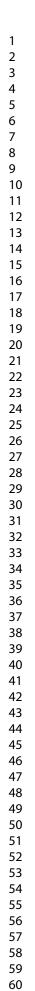
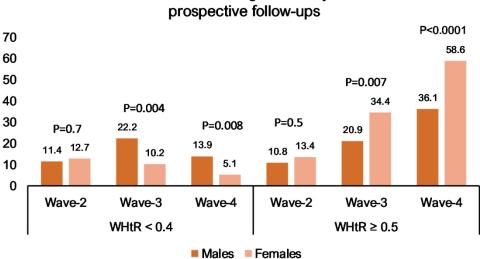


Figure 1. Percentages of underweight and overweight/obese participants by sex. For classification, age and sex specific cut-off points were used for participants under 18 years of age at follow-up. For participants aged 18 and over, underweight was classified as BMI < 18,5; normal weight as 18,5-24,99; overweight as 25-29,99 and obesity as ≥ 30 .

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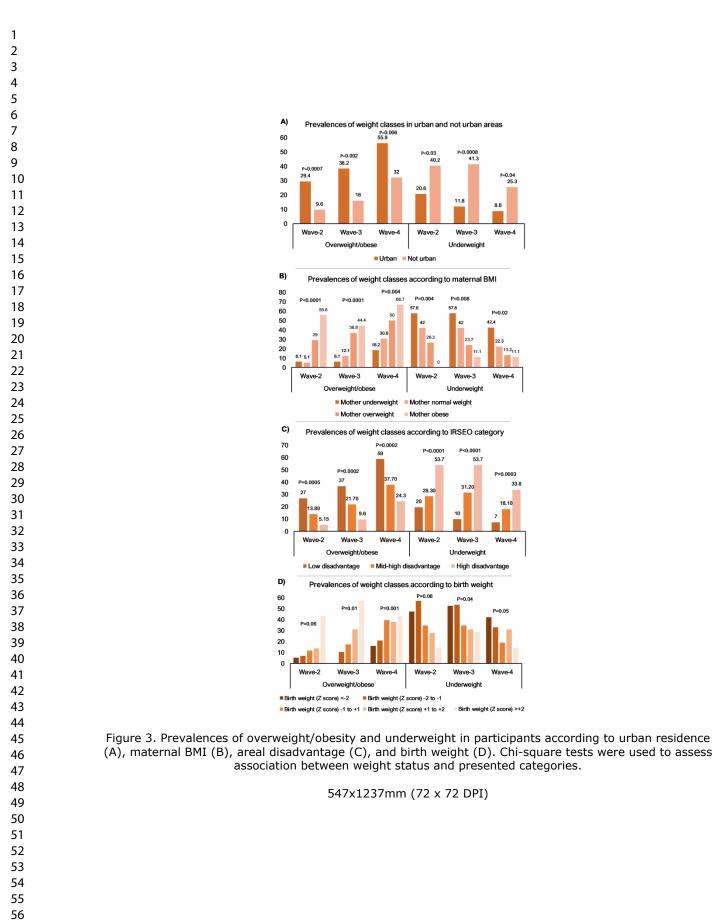




Prevalences of low and high WHtR by sex in three

Figure 2. Prevalences for low and high waist-to-height ratio at three time points according to sex. P-values were calculated with chi-square tests and represent differences between sexes. Values are in percentages.

127x76mm (300 x 300 DPI)



	Participants (N=315)	Dropouts (N=371)	P-value
Males (%)	50.2	53.1	P=0.44
Urban residence (%)	10.8	31.8	P<0.0001
Birthweight, z score	-0.29	-0.30	P=0.95
IRSEO score	80.8	65.9	P<0.0001
Maternal BMI	22.2	22.3	P=0.71

Comparison between participants and dropouts. Values for categorical variables (sex, urban residence) are presented in percentages and values for continuous variables in means. Chisquare tests were used for analysis of categorical variables and t-tests for continuous variables.

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STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	2
		(<i>b</i>) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			1
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(<i>a</i>) Give the eligibility criteria, and the sources and methods of selection of	5
	-	participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	6-7
		effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	6-7
measurement		assessment (measurement). Describe comparability of assessment methods if	
D.	0	there is more than one group	5, 1
Bias	9	Describe any efforts to address potential sources of bias	5
Study size Quantitative variables	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(<i>a</i>) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, explain how loss to follow-up was addressed	
		(<u>e</u>) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially	5
		eligible, examined for eligibility, confirmed eligible, included in the study,	
		completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	tabl
		and information on exposures and potential confounders	1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	tabl

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16	(a) Cive up adjusted estimates and if applicable confounder adjusted estimates and their	8-10
16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their	
	(b) Report category boundaries when continuous variables were categorized	
	(c) If relevant, consider translating estimates of relative risk into absolute risk for a	
	meaningful time period	
17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity	
	analyses	
18	Summarise key results with reference to study objectives	10- 11
19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.	12
	Discuss both direction and magnitude of any potential bias	
20	Give a cautious overall interpretation of results considering objectives, limitations,	11-
	multiplicity of analyses, results from similar studies, and other relevant evidence	12
21	Discuss the generalisability (external validity) of the study results	12
on		
	17 18 19 20 21	 precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period 17 Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses 18 Summarise key results with reference to study objectives 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence 21 Discuss the generalisability (external validity) of the study results

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

applicable, for the original study on which the present article is based