Growth and body composition of children aged two to four years after exposure to community mobilisation women's groups in Bangladesh.

Edward Fottrell PhD1** e.fottrell@ucl.ac.uk

Naveed Ahmed MBBS^{2*} naveedahmed225@gmail.com

Badrun Nahar MSc² <u>bithipcp@dab-bd.org</u>

Sanjit Kumer Shaha MSS² sanjitpcp@dab-bd.org

Abdul Kuddus MBBS MPH² kudduspcp@dab-bd.org

Carlos Grijalva-Eternod MSc¹c.eternod@ucl.ac.uk

Tasmin Nahar MSS² tasminpcp@dab-bd.org

Caroline Fall FRCPCH³ chdf@mrc.soton.ac.uk

Clive Osmond PhD³ <u>co@mrc.soton.ac.uk</u>

Virginia Govoni MSc⁴ v.govoni@qmul.ac.uk

Sarah Finer PhD⁴ <u>s.finer@qmul.ac.uk</u>

Chittaranjan Yajnik FRCP⁵ csyajnik@gmail.com

AK Azad Khan DPhil² president@dab-bd.org

Anthony Costello FMedSci^{1,6} cihdcostello@gmail.com

Kishwar Azad FCPS^{2^} kishwar.azad@googlemail.com

Graham A Hitman FRCP^{4^} g.a.hitman@qmul.ac.uk

1. UCL Institute for Global Health, University College London, UK

2. Diabetic Association of Bangladesh Perinatal Care Project, Dhaka, Bangladesh

3. MRC Lifecourse Epidemiology Unit, University of Southampton, UK

4. Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary

University of London, UK

- 5. Diabetes Unit, King Edward Memorial Hospital, Pune, India
- 6. WHO Department of Maternal, Newborn, Child and Adolescent Health, Geneva,

Switzerland

*Joint first authors

^Joint senior authors

+Corresponding author

Correspondence to: Dr Edward Fottrell, UCL Institute for Global Health, 30 Guilford Street,

London, WC1N 1EH, United Kingdom. <u>e.fottrell@ucl.ac.uk</u>

Manuscript word count: 2999

Key words: developing countries; Bangladesh; children; growth; life-course/childhood circumstances; public health; social and life-course epidemiology.

Abstract

Background

Women's groups interventions in Bangladesh reduced neonatal deaths by 38% and improved hygienic delivery, newborn care practices and breastfeeding. We explore the longer-term impact of exposure to women's groups during pregnancy on child growth at two to four years.

Methods

We performed a cross-sectional survey of child anthropometric measures (analysed as zscores) among children born to women who had participated in the women's groups interventions whilst pregnant, compared to an age- and sex-matched sample of children born to control mothers. Results were stratified by maternal BMI and adjusted for possible confounding effects of maternal education, household asset ownership and, in a separate model, mother-child height difference, a proxy for improved survival of small babies in intervention groups.

Results

Data were obtained from 2587 mother-child pairs (91% response). After adjustment for asset ownership, maternal education and potential survival effects, children whose mothers were exposed to the women's group intervention had higher head (0.16 (0.04-0.28)), midupper arm (0.11 (0.04-0.19)), abdominal (0.13 (0.00-0.26)) and chest (0.18 (0.08-0.29)) circumferences than their control counterparts. No significant differences in subcutaneous fat (sub-scapular and triceps skinfold thickness) were observed. When stratified by maternal BMI, intervention children had higher weight, BMI and circumferences, and these effects decreased with increasing maternal BMI category.

Conclusions

Women's groups appear to have had a lasting, positive impact on child anthropometric

outcomes, with most significant results clustering in children of underweight mothers.

Observed differences are likely to be of public health significance in terms of the nutritional

and metabolic development of children.

What is already known on this subject?

Foetal and early life exposures impact on child growth, development and subsequent disease risk. Interventions that act during periconceptual and postnatal periods of development therefore have the potential to influence longer-term growth and health outcomes. Participatory women's groups (PWG) community mobilisation interventions have been shown to improve neonatal survival as well as essential newborn care practices in resource-poor settings, including Bangladesh. PWG interventions act during critical windows of growth and development yet their lasting effects on child growth have not been studied.

What this study adds?

Through a large follow-up study of children in rural Bangladesh, we observe that maternal exposure to PWG interventions during pregnancy may improve child lean mass growth markers at 2-4 years. The observed growth differences are likely to be significance in terms of the nutritional and metabolic development of Bangladeshi children.

Background

The initial years of life are critical for adequate physical, cognitive, motor and socioemotional development[1]. Further, a range of metabolic, immunological and physiological adaptations to early-life exposures are known to modify subsequent disease risk[2-6]. Child growth is therefore an important indicator of development as well as future disease risk, and is a crucial target for intervention. Low- and middle-income countries are facing a 'dual burden' of prevalent underweight and overweight[7], alongside a rapidly growing burden of diabetes and cardio-metabolic diseases[8]. Therefore population-scale intervention strategies are urgently needed across the life-course, tailored to critical windows of exposure and opportunity, such as peri-conception to postnatal life.

Participatory women's groups (PWG) community mobilisation interventions have been widely studied in the context of neonatal mortality, but their potential to affect childhood development remains unknown. One such PWG intervention, originally delivered in rural Bangladesh in 2009-2011 as part of a cluster randomised controlled trial, covered approximately 46,000 reproductive-aged women (15-49 years) during preconception, pregnancy and the postpartum period. The intervention showed a 38% reduction in neonatal mortality, and improved hygienic delivery and essential newborn care practices[9]. It used a participatory learning and action (PLA) cycle of monthly meetings facilitated by lay women. In the PLA cycle, women themselves identify and prioritise local health challenges, and then design, implement and evaluate their own solutions. The initial intervention and evaluation focused on neonatal mortality, but the PWGs continued to meet and focused on child health and women's and reproductive health, with encouraging results regarding breastfeeding, nutritional practices and hygiene[10, 11].

In this formative study, we followed up children (now aged 24-48 months) born to women exposed to the PWG intervention and compare them to a random sample of age- and sexmatched children born to control mothers (i.e. unexposed to PWGs) to explore possible impact on child growth.

Methods

Study design and participants

The original PWG trial and this follow-up cross-sectional survey were located in 18 purposefully selected rural unions in Faridpur, Bogra and Moulavibazar districts in Bangladesh. Each union served as a cluster, and was randomly allocated to either intervention or control (nine in each) as described elsewhere[9, 12]. Between 2008 and 2012, all births in the study areas were recorded using an incentivised key-informant system, with women interviewed about their pregnancy, childbirth and postpartum experiences between six and 52 weeks after delivery. These interviews also recorded women's PWG participation. The data formed the sampling frame from which current study participants were selected.

In intervention clusters, women (and their children) were eligible for follow-up if they met certain criteria: had permanently resided in the study cluster; attended at least six consecutive PWG meetings during the intervention prior to giving birth to a live, singleton baby between October 2009 and June 2011; and had been successfully interviewed in the routine postpartum survey six to 52 weeks after delivery. These women were identified from the trial database and triangulated with registers maintained by PWG facilitators throughout the intervention, resulting in a target of 1,347 eligible participants from a total of 12,131 births registered in the intervention clusters between October 2009 and June

2011 (11%). In control areas, participants were women (and their child) who met the equivalent criteria, but had never attended or heard of the PWG intervention. The control sample was randomly selected from the trial database, and was matched for age and sex of children in the intervention population. The control population was oversampled by 10% to allow for an expected higher rate of refusals and loss to follow-up, giving a target control sample of 1,487.

Procedures and outcomes

Data were collected between July and October 2013. Study participants were visited at home by one of seven trained fieldworkers who administered structured questionnaires on duration of breastfeeding and age at introduction of solid foods. Anthropometric measures of the children were taken using a standard protocol, including: shoeless, standing height using a portable stadiometer (Microtoise); weight wearing only light clothing and recorded using digital weighing scales (TANITA); head, chest, abdominal and mid-upper arm circumferences using measuring tapes (LASSO and MUAC); and triceps and subscapular skinfold thickness using callipers (HOLTAIN). All measures, except weight and height, were taken in duplicate, with the average used in the analysis. The weight and height of women was also recorded.

All fieldworkers, educated to at least undergraduate level, were trained for seven days on survey administration and anthropometric measurements by three experienced consultant paediatricians at the Department of Paediatrics and Neonatology, BIRDEM Hospital, Dhaka. This included in-situ praxis with children matching the study age range and assessment of inter- and intra-observer measurement variability. Fieldworkers completed another sevenday refresher course one month later, followed by a seven-day pilot session in a rural

setting outside the study area to validate their work. Finally, all fieldworker measurements were directly supervised during the first week of actual data collection, with errors corrected and discussed.

Data were recorded onto paper forms and entered into an Access database in Dhaka. Implausible data were cross-checked with the original survey tools and referred back to the field for correction. Survey and anthropometric data were linked to the socio-economic and background data already recorded in the previous trial evaluation.

Statistical analysis

Following data cleaning, only records with non-missing and plausible mother and child anthropometric measurements were included in the analysis. Analyses were performed using Stata (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). Anthropometric z-scores were calculated using the 2016 WHO growth standards for height, weight, body mass index (BMI), weight-for-height, head circumference, mid-upper arm circumference, triceps, and subscapular skinfold thickness. Internal z-scores were created for chest and abdominal circumference measures by pooling all measures, adjusting to the median age of the sample using simple linear regression, converting these adjusted values by subtracting the subject mean from the population mean, and dividing the result by the population standard deviation; this was done separately for males and females.

Random effects linear regression was applied to compare cluster mean child anthropometry between the intervention and control groups. Interactions between child anthropometric outcomes and maternal BMI were explored. Maternal BMI categories appropriate for South Asian populations were used: less than 18.5kg/m² for underweight, 18.5 to less than 23 for

normal weight, and 23 or more for overweight[13]. Our analysis indicated significant interaction effects, thus results are presented stratified by the three maternal BMI categories.

To understand anthropometric differences between study arms, we present crude results that account for the stratified, clustered survey design (supplementary table 1 shows intracluster correlation coefficients). To understand whether any of the observed differences can be explained by socioeconomic factors, we ran a multivariate regression model (Model 1) adjusting for maternal education and household asset ownership – variables identified as differing significantly between the study arms and also observed to be associated with at least one of the child anthropometric measures.

In a separate regression model (Model 2), results were also adjusted for the difference in mother-child height z-score to understand whether any of the anthropometric differences observed at 24-48 months could be explained by a PWG intervention survival effect at birth[9]. Underlying this is the assumption that observed intervention effects on neonatal mortality resulted in the survival of children with lower birth weights[14], and that in the absence of this survival effect, the mean mother-child height difference would be similar in the study arms. Adjustment for the difference in mother-child height z-score therefore removes any potential survival effects. Difference in mother-child height z-score was obtained by subtracting the child height z-score from the maternal height z-score.

Results

Survey and anthropometric data were collected from 1,264 children and their mothers in intervention clusters and 1,323 children and their mothers in control areas ((94% and 89% response rates, respectively). Reasons for attrition mainly relate to non-eligibility at the time

of the survey (i.e. migration/non-permanent residence (n=246), child or mother's death (n=31), or child born outside the target period (n=1)). Only 11 eligible individuals refused to participate in the survey.

27 intervention cases (2.1%) and 86 control cases (6.5%) with incomplete anthropometric data were removed from the analysis, giving a final sample of 2,517 mother-child pairs (1,280 control, 1,237 intervention).

Table 1 shows the cluster-level mean measures of socioeconomic and demographic characteristics by study arm. These data indicate that exposed mothers were significantly older, less well-educated and owned fewer household assets on average. The difference in mother-child height z-scores was greater in the intervention clusters. There were no significant differences in maternal BMI or BMI category between intervention arms, with overall prevalence of underweight, normal weight and overweight being 28.7%, 46.8% and 24.5%, respectively. Table 2 shows the absolute values of anthropometric measures by gender and control and intervention group.

Table 3 shows the pooled cluster mean anthropometric z-scores for children aged 24 to 48 months by intervention exposure group. Unadjusted values show children in the intervention arm having significantly lower weight-for-age z-scores (WAZ) and height-for-age z-scores (HAZ). Differences in mother-child height z-scores are also observed, with this difference being significantly greater in the intervention population even after adjustment for socioeconomic factors. After adjustment for asset ownership and maternal education (Model 1), differences in WAZ and HAZ were attenuated and only remain statistically significant for HAZ. Additional adjustment for mother-child height difference z-scores (Model 2) further attenuates and removes significant effects in WAZ and HAZ. However,

differences in body circumferences (head, upper arm, abdomen, and chest) are increased, significantly, among exposed individuals (Table 3 & Figure 1a). No significant differences between groups were observed for subcutaneous fat (sub-scapular and triceps skinfold thickness).

Table 1 Cluster level mean socioeconomic and demographic characteristics of the study population by control and intervention clusters and random effects regression coefficients.

		Control (n=1,280)	Intervention (n=1,237)	Difference	
Respondent characteristics		mean/% (95% CI)	mean/% (95% CI)	diff ¹ (95% CI)	p-value
Religion, %					
Islam		89.3 (83.4; 95.3)	88.5 (82.6; 94.5)	-0.01 (-0.07; 0.05)	0.818
Economic status, %					
None		18.4 (13.0; 23.7)	22.8 (17.5; 28.2)	0.04 (-0.01; 0.10)	0.106
	One	23.6 (18.1; 29.1)	25.3 (19.8; 30.8)	0.02 (-0.04; 0.07)	0.550
	Two	14.5 (11.3; 17.6)	16.9 (13.8; 20.1)	0.02 (-0.01; 0.06)	0.127
	Three	43.6 (35.9; 51.3)	34.7 (27.1; 42.4)	-0.09 (-0.17; -0.01)	0.025
Maternal educat					
	or less than 1 year	16.6 (10.5; 22.7)	19.6 (13.5; 25.7)	0.03 (-0.03; 0.09)	0.333
	Primary (any level)	33.3 (27.8; 38.9)	43.3 (37.8; 48.9)	0.10 (0.04; 0.16)	0.001
	condary and higher	50.0 (45.2; 54.8)	37.6 (32.7; 42.4)	-0.12 (-0.17; -0.07)	<0.001
Maternal literacy					
	y or with difficulty)	79.7 (73.2; 86.2)	75.0 (68.5; 81.5)	-0.05 (-0.11; 0.02)	0.161
Maternal charact	eristics	mean/% (95% CI)	mean/% (95% CI)	diff ¹ (95% CI)	p-value
Age, years		27.1 (26.4; 27.8)	27.9 (27.2; 28.6)	0.81 (0.09; 1.53)	0.026
Height, cm		150.6 (150.1; 151.0)	150.7 (150.2; 151.1)	0.14 (-0.31; 0.58)	0.551
Weight, kg		47.8 (46.5; 49.2)	46.7 (45.3; 48.0)	-1.14 (-2.51; 0.23)	0.103
BMI, kg/m ²		21.1 (20.5; 21.6)	20.5 (20.0; 21.1)	-0.53 (-1.08; 0.03)	0.063
	Underweight	27.0 (20.9; 33.2)	30.4 (24.2; 36.5)	0.03 (-0.03; 0.10)	0.297
BMI Category	Normal	46.0 (42.2; 49.9)	47.6 (43.7; 51.5)	0.02 (-0.02; 0.05)	0.421
	Overweight	27.2 (21.7; 32.6)	21.7 (16.2; 27.1)	-0.05 (-0.11; 0.00)	0.053
Height, z-scores		-1.9 (-2.0; -1.9)	-1.9 (-2.0; -1.8)	0.02 (-0.05; 0.09)	0.552
Children's characteristics		mean/% (95% CI)	mean/% (95% CI)	diff ¹ (95% CI)	p-value
Age, months		35.2 (34.3; 36.2)	35.0 (34.1; 36.0)	-0.18 (-1.16; 0.80)	0.716
Male sex, %		53.5 (49.7; 57.4)	53.3 (49.4; 57.2)	-0.00 (-0.04; 0.04)	0.901
Duration of breastfeeding, months		28.9 (28.1; 29.7)	29.4 (28.5; 30.2)	0.47 (-0.37; 1.31)	0.277
Mother-child hei	ght diff, z-score	0.0 (-0.2; 0.1)	0.2 (0.0; 0.3)	0.22 (0.07; 0.36)	0.003

¹ Regression coefficient. Difference (diff).

Table 2 Cluster means absolute measures of anthropometric outcomes for children (males and females) aged from 24 to48 months by intervention exposure.

	MaleControlIntervention(n=685)(n=659)		Ferr	nale	Total		
			Control Intervention (n=595) (n=578)		Control (n=1280)	Intervention (n=1237)	
	mean (95%Cl)	mean (95%CI)	mean (95%Cl)	mean (95%CI)	mean (95%Cl)	mean (95%CI)	
Weight, kg	11.8 (11.5; 12.1)	11.6 (11.3; 11.9)	11.1 (10.8; 11.4)	10.9 (10.6; 11.2)	11.4 (11.2; 11.7)	11.3 (11.0; 11.5)	
Height, cm	89.1 (88.0; 90.1)	87.9 (86.9; 89.0)	87.1 (86.0; 88.3)	86.6 (85.5; 87.8)	88.2 (87.3; 89.1)	87.3 (86.4; 88.3)	
BMI	14.8 (14.7; 14.9)	14.9 (14.8; 15.1)	14.5 (14.3; 14.7)	14.5 (14.3; 14.7)	14.7 (14.6; 14.8)	14.7 (14.6; 14.8)	
Head circumference, cm	47.1 (46.8; 47.4)	47.1 (46.9; 47.4)	45.9 (45.6; 46.2)	46.1 (45.8; 46.4)	46.6 (46.3; 46.8)	46.7 (46.4; 46.9)	
MUAC, cm	14.5 (14.4; 14.7)	14.6 (14.4; 14.7)	14.3 (14.1; 14.5)	14.3 (14.1; 14.5)	14.4 (14.3; 14.5)	14.4 (14.3; 14.6)	
Abdominal circumference, cm	46.1 (45.5; 46.6)	46.3 (45.7; 46.8)	45.5 (45.1; 45.9)	45.5 (45.1; 46.0)	45.8 (45.3; 46.2)	45.9 (45.5; 46.4)	
Chest circumference, cm	47.8 (47.4; 48.3)	48.2 (47.7; 48.6)	46.8 (46.4; 47.3)	46.9 (46.4; 47.3)	47.4 (47.0; 47.8)	47.6 (47.2; 47.9)	
Sub-scapular, cm	5.5 (5.2; 5.7)	5.5 (5.3; 5.8)	5.8 (5.5; 6.2)	5.8 (5.4; 6.1)	5.6 (5.3; 5.9)	5.7 (5.4; 6.0)	
Triceps, cm	7.3 (7.1; 7.6)	7.5 (7.2; 7.8)	7.6 (7.2; 8.1)	7.6 (7.1; 8.0)	7.5 (7.1; 7.8)	7.5 (7.2; 7.9)	
Mother-child height difference, cm	61.8 (61.0; 62.6)	62.5 (61.7; 63.4)	63.0 (62.3; 63.8)	64.3 (63.5; 65.0)	62.4 (61.7; 63.1)	63.3 (62.6; 64.1)	

	Control (n=1280)	Intervention (n=1237)	Crude difference		Model 1		Model 2	
	mean (95%CI)	mean (95%CI)	diff1 (95% CI)	р	diff1 (95% CI)	р	diff1 (95% CI)	р
Weight-for-age	-1.68 (-1.77; -1.6)	-1.81 (-1.89; -1.72)	-0.12 (-0.21; -0.04)	0.005	-0.08 (-0.16; 0.01)	0.078	0.01 (-0.06; 0.07)	0.860
Height-for-age	-1.8 (-1.96; -1.64)	-2.0 (-2.16; -1.84)	-0.20 (-0.36; -0.04)	0.014	-0.15 (-0.28; -0.02)	0.022	-0.02 (-0.10; 0.06)	0.651
Weight-for-height	-0.96 (-1.05; -0.88)	-0.97 (-1.05; -0.89)	-0.01 (-0.09; 0.08)	0.877	0.01 (-0.07; 0.09)	0.760	0.02 (-0.06; 0.10)	0.657
BMI	-0.77 (-0.86; -0.67)	-0.74 (-0.83; -0.64)	0.03 (-0.07; 0.13)	0.528	0.04 (-0.04; 0.12)	0.357	0.02 (-0.06; 0.10)	0.577
Head circumference	-1.64 (-1.83; -1.46)	-1.57 (-1.75; -1.39)	0.07 (-0.11; 0.25)	0.447	0.11 (-0.06; 0.27)	0.212	0.16 (0.04; 0.28)	0.007
MUAC	-1.05 (-1.17; -0.93)	-1.0 (-1.11; -0.88)	0.06 (-0.06; 0.17)	0.355	0.07 (-0.00; 0.15)	0.066	0.11 (0.04; 0.19)	0.004
Abdominal circumference	-0.04 (-0.2; 0.11)	0.02 (-0.13; 0.18)	0.06 (-0.09; 0.22)	0.422	0.08 (-0.08; 0.25)	0.336	0.13 (0.00; 0.26)	0.048
Chest circumference	-0.05 (-0.2; 0.1)	0.04 (-0.11; 0.19)	0.09 (-0.06; 0.24)	0.233	0.11 (-0.07; 0.30)	0.224	0.18 (0.08; 0.29)	< 0.001
Sub-scapular	-0.44 (-0.75; -0.14)	-0.39 (-0.69; -0.08)	0.06 (-0.25; 0.36)	0.723	0.08 (-0.24; 0.41)	0.628	0.09 (-0.21; 0.39)	0.558
Triceps	-0.41 (-0.64; -0.19)	-0.35 (-0.57; -0.12)	0.06 (-0.16; 0.29)	0.577	0.07 (-0.16; 0.30)	0.532	0.08 (-0.16; 0.33)	0.502
Mother-child height diff.	-0.04 (-0.19; 0.1)	0.17 (0.03; 0.31)	0.22 (0.07; 0.36)	0.003	0.19 (0.06; 0.32)	0.006	na	na

Table 3 Overall anthropometric z-scores for children (males and females) aged from 24 to 48 months. Regression coefficients derived from random effects linear regression models intervention effect.

All values are expressed in z-scores. Crude differences accounted for the stratified and clustered design.

¹ Regression coefficient. Difference (diff).

Model 1 Adjusted for maternal education, household asset ownership

Model 2 Adjusted for maternal education, household asset ownership and mother-child height z-score difference

A significant interaction effect between the intervention and maternal BMI is observed in six of the ten anthropometric outcomes (supplementary Table S2), and therefore the analysis is stratified by maternal BMI group, with summary z-score measures presented in Figure 1b and regression results shown in Tables 4a-c. Three interesting patterns arise. First, in children exposed to PWG, there is an apparent trend denoting greater WAZ, WHZ, BMI and body circumferences, but this effect decreases with increasing maternal BMI category (Figure 1b). We do not observe this or any trend with measures of tallness (HAZ) or fatness (skinfolds). Second, most of the observed adjusted differences between study arms that reached statistical significance are clustered among those in the underweight maternal BMI category, although some are also observed in the middle BMI category. After controlling for potential survival effect (Model 2), no significant differences are observed in the overweight maternal BMI category. Lastly, the significant differences in childhood measurements that persisted after adjustment for maternal education and wealth, as well as survival effect, are clustered in anthropometric indices denoting heaviness (WAZ, WHZ, BMI, MUAC, AC, HC and CC) rather than tallness (HAZ) or fatness (skinfolds).

Table 4 Cluster mean	anthropometric z-	-scores for children (males and remales	aged fro	m 24 to 48 months	by matern	al Bivil category.	
a) Maternal BMI<18.5	Control (n=344)	Intervention. (n=384)	n=384) Crude difference N		Model 1		Model 2	
	Mean (95%CI)	Mean (95%CI)	diff1 (95% CI)	p-value	diff1 (95% CI)	p-value	diff1 (95% CI)	p-value
Weight-for-age	-2.1 (-2.2; -2.0)	-2.1 (-2.2; -1.9)	0.02 (-0.12 - 0.16)	0.744	0.04 (-0.10 - 0.18)	0.537	0.10 (-0.02 - 0.22)	0.118
Height-for-age	-2.1 (-2.2; -1.9)	-2.2 (-2.3; -2.0)	-0.14 (-0.30 - 0.02)	0.080	-0.11 (-0.27 - 0.05)	0.165	-0.02 (-0.14 - 0.09)	0.666
Weight-for-height	-1.3 (-1.5; -1.2)	-1.2 (-1.3; -1.0)	0.15 (0.00 - 0.29)	0.044	0.15 (0.01 - 0.30)	0.039	0.15 (0.01 - 0.30)	0.037
BMI	-1.1 (-1.3; -1.0)	-0.9 (-1.1; -0.8)	0.18 (0.02 - 0.34)	0.024	0.18 (0.03 - 0.33)	0.019	0.17 (0.02 - 0.32)	0.029
Head circumference	-1.8 (-2.0; -1.7)	-1.6 (-1.8; -1.5)	0.20 (0.06 - 0.34)	0.005	0.21 (0.07 - 0.35)	0.003	0.24 (0.10 - 0.38)	0.001
MUAC	-1.3 (-1.4; -1.2)	-1.2 (-1.3; -1.1)	0.12 (-0.01 - 0.25)	0.075	0.12 (-0.00 - 0.24)	0.056	0.14 (0.03 - 0.26)	0.014
Abdominal circumference	-0.4 (-0.6; -0.1)	-0.1 (-0.3; 0.1)	0.23 (0.02 - 0.44)	0.031	0.24 (0.07 - 0.41)	0.005	0.27 (0.10 - 0.44)	0.002
Chest circumference	-0.3 (-0.6; -0.1)	-0.1 (-0.4; 0.1)	0.20 (-0.07 - 0.47)	0.147	0.22 (0.00 - 0.43)	0.050	0.26 (0.10 - 0.42)	0.001
Sub-scapular	-0.6 (-0.9; -0.3)	-0.5 (-0.9; -0.2)	0.07 (-0.28 - 0.42)	0.703	0.06 (-0.13 - 0.24)	0.548	0.06 (-0.13 - 0.26)	0.530
Triceps	-0.5 (-0.8; -0.3)	-0.4 (-0.7; -0.2)	0.08 (-0.17 - 0.33)	0.518	0.03 (-0.10 - 0.16)	0.644	0.03 (-0.10 - 0.16)	0.636
Mother-child height diff.	0.2 (0.0; 0.4)	0.4 (0.2; 0.5)	0.15 (-0.02 - 0.33)	0.084	0.16 (0.04 - 0.29)	0.010	na	na
b) Maternal BMI 18.5 to <23	Control (n=589)	Intervention. (n=589)	Crude differen	се	Model 1		Model 2	
	Mean (95%CI)	Mean (95%CI)	diff1 (95% CI)	p-value	diff ¹ (95% CI)	p-value	diff1 (95% CI)	p-value
Weight-for-age	-1.7 (-1.8; -1.6)	-1.8 (-1.9; -1.7)	-0.07 (-0.18 - 0.04)	0.200	-0.04 (-0.15 - 0.07)	0.454	0.02 (-0.08 - 0.11)	0.710
Height-for-age	-1.8 (-2.0; -1.7)	-2.0 (-2.2; -1.9)	-0.15 (-0.300.00)	0.050	-0.12 (-0.28 - 0.05)	0.174	-0.01 (-0.17 - 0.15)	0.901
Weight-for-height	-0.9 (-1.1; -0.8)	-0.9 (-1.0; -0.8)	0.04 (-0.11 - 0.19)	0.588	0.04 (-0.07 - 0.16)	0.449	0.03 (-0.08 - 0.15)	0.567
BMI	-0.7 (-0.9; -0.6)	-0.7 (-0.8; -0.5)	0.07 (-0.10 - 0.24)	0.422	0.06 (-0.06 - 0.19)	0.298	0.04 (-0.08 - 0.16)	0.532
Head circumference	-1.7 (-1.9; -1.4)	-1.5 (-1.8; -1.3)	0.11 (-0.14 - 0.36)	0.400	0.14 (-0.07 - 0.36)	0.199	0.18 (0.02 - 0.34)	0.027
MUAC	-1,0 (-1.2; -0.9)	-1.0 (-1.1; -0.8)	0.08 (-0.05 - 0.21)	0.237	0.08 (-0.01 - 0.17)	0.067	0.11 (0.02 - 0.20)	0.015
Abdominal circumference	-0.1 (-0.2; 0.1)	0.1 (-0.1; 0.3)	0.12 (-0.07 - 0.31)	0.211	0.13 (-0.06 - 0.33)	0.183	0.16 (-0.02 - 0.34)	0.079
Chest circumference	-0.1 (-0.2; 0.1)	0.1 (-0.1; 0.3)	0.16 (-0.02 - 0.34)	0.079	0.18 (-0.01 - 0.38)	0.062	0.22 (0.04 - 0.39)	0.017
Sub-scapular	-0.4 (-0.7; -0.2)	-0.4 (-0.6; -0.1)	0.09 (-0.18 - 0.37)	0.505	0.11 (-0.12 - 0.33)	0.358	0.10 (-0.10 - 0.30)	0.325
Triceps	-0.4 (-0.6; -0.2)	-0.3 (-0.5; -0.1)	0.07 (-0.15 - 0.29)	0.547	0.07 (-0.11 - 0.25)	0.459	0.07 (-0.12 - 0.26)	0.456
Mother-child height diff.	0.0 (-0.1; 0.1)	0.2 (0.0; 0.3)	0.16 (0.04 - 0.29)	0.010	0.15 (0.02 - 0.28)	0.021	na	na
c) Maternal BMI <u>></u> 23	Control (n=347)	Intervention. (n=264)	Crude differen	се	Model 1		Model 2	
	Mean (95%CI)	Mean (95%CI)	diff ¹ (95% CI)	p-value	diff1 (95% CI)	p-value	diff1 (95% CI)	p-value
Weight-for-age	-1.3 (-1.4; -1.1)	-1.5 (-1.7; -1.4)	-0.27 (-0.450.09)	0.003	-0.22 (-0.390.05)	0.011	-0.08 (-0.23 - 0.07)	0.320
Height-for-age	-1.5 (-1.7; -1.2)	-1.7 (-2.0; -1.5)	-0.25 (-0.480.03)	0.027	-0.21 (-0.46 - 0.05)	0.108	-0.01 (-0.14 - 0.13)	0.908
Weight-for-height	-0.6 (-0.8; -0.5)	-0.8 (-1.0; -0.6)	-0.17 (-0.320.02)	0.031	-0.14 (-0.30 - 0.02)	0.077	-0.11 (-0.27 - 0.06)	0.211

Table 4 Cluster mean anthropometric z-scores for children (ma	nales and females) aged from 24 to 48 months by	/ maternal BMI category.
---	---	--------------------------

BMI	-0.5 (-0.6; -0.3)	-0.6 (-0.8; -0.4)	-0.14 (-0.30 - 0.03)	0.099	-0.11 (-0.28 - 0.05)	0.184	-0.11 (-0.27 - 0.06)	0.209
			1 /		. ,		()	
Head circumference	-1.4 (-1.6; -1.2)	-1.5 (-1.7; -1.3)	-0.07 (-0.28 - 0.14)	0.533	-0.04 (-0.25 - 0.17)	0.701	0.02 (-0.20 - 0.25)	0.828
MUAC	-0.8 (-0.9; -0.6)	-0.8 (-0.9; -0.6)	-0.01 (-0.15 - 0.13)	0.855	0.02 (-0.13 - 0.16)	0.821	0.09 (-0.04 - 0.21)	0.192
Abdominal circumference	0.3 (0.1; 0.5)	0.2 (0.0; 0.3)	-0.12 (-0.30 - 0.07)	0.217	-0.11 (-0.32 - 0.10)	0.303	-0.02 (-0.23 - 0.18)	0.820
Chest circumference	0.3 (0.0; 0.5)	0.2 (-0.1; 0.4)	-0.08 (-0.33 - 0.17)	0.519	-0.03 (-0.25 - 0.19)	0.776	0.06 (-0.17 - 0.28)	0.620
Sub-scapular	-0.2 (-0.6; 0.1)	-0.3 (-0.7; 0.1)	-0.07 (-0.45 - 0.32)	0.732	-0.03 (-0.37 - 0.31)	0.869	0.00 (-0.35 - 0.35)	0.998
Triceps	-0.3 (-0.6; 0.0)	-0.3 (-0.6; 0.0)	0.02 (-0.26 - 0.30)	0.897	0.04 (-0.21 - 0.29)	0.754	0.07 (-0.20 - 0.33)	0.621
Mother-child height diff.	-0.4 (-0.6-0.2)	-0.1 (-0.3; 0.1)	0.32 (0.14 - 0.50)	<0.001	0.28 (0.10 - 0.45)	0.002	na	na

All values are expressed in z-scores. Crude differences accounted for the stratified and clustered design. ¹ Regression coefficient. Difference (diff).

Model 1 Adjusted for maternal education, household asset ownership

Model 2 Adjusted for maternal education, household asset ownership and mother-child height z-score difference

Discussion

Two years after a PWG intervention that reduced neonatal mortality and improved essential newborn care practices, we observed growth differences in children from mothers actively participating in the intervention, compared to a random sample of children from nonexposed mothers. First, the difference in mother and child height at 24-48 months is greater among those in intervention areas, which we postulate may be attributed to increased neonatal survival of smaller children in this exposed population. Second, children from exposed mothers had lower height z-scores than their non-exposed counterparts, but, after adjusting for the survival effect on size (Model 2), these children were no longer shorter but had greater body circumferences than their counterparts. This denotes greater heaviness, albeit with similar skinfold values, indicating similar subcutaneous fat storage. Third, when stratifying these adjusted comparisons by current maternal BMI categories, the positive effects of the PWG intervention observed in growth indicators denoting heaviness (i.e. BMI, WHZ or body circumferences) clusters in children of underweight mothers, although some significant differences are also found in those with mothers with normal BMI. Lastly, and despite not all differences being significant, we observe that children exposed to PWG from underweight mothers had greater anthropometric values than their non-exposed counterparts, whilst there is no clear association in children from overweight mothers.

The significance of our findings from a post-hoc analysis require cautious consideration. Overall, the significant adjusted increases observed in anthropometric indices range from 0.11 to 0.18 z-scores in the overall study sample, and from 0.14 to 0.27 z-scores in children from underweight mothers. Using a mean WHZ value of -0.9, taken from the Bangladesh 2014 Demographic and Health Survey[15], and assuming a normal distribution with a

standard deviation of 1-score, the observed difference could translate into a reduction in prevalence of wasting from 13.6% to 11.3% and up to 10.0% if we use our study sample range, or a reduction to 10.7% and up to a 8.5% among those born to underweight mothers. It is important to bear in mind that the objective of the original PWG intervention was neonatal survival, not longer-term child growth and so the potential public health impact of PWG interventions for reducing malnutrition prevalence and improving child growth requires further exploration.

The observed improvements in anthropometric indices might also have implications for adult health. The significant increase in head circumference, especially for underweight mothers, could reflect important effects on brain growth in infancy, although other explanations are possible including increased growth of the bony skull or extra-cranial adiposity. This finding warrants more detailed study as poor cognitive outcomes and educational performance are among the most important results of infant malnutrition. The significant increase of anthropometric indices denoting heaviness, such as BMI or body circumferences without a concurrent increase in anthropometric indices denoting fatness, strongly suggest that these gains primarily reflect gains in lean mass such as muscle, bone or organs. Furthermore, these significant gains seem clustered among children who might have been exposed to an undernourished niche during development, as represented by a low maternal BMI. Given the wealth of epidemiological literature on the long-term adverse effects of maternal undernutrition on offspring health in later life[3, 4], including in Bangladesh[16], further studies are imperative to determine whether the observed changes could also translate into improved metabolic, cognitive and physiological function. The current findings lack evidence to support a possible beneficial effect of the same intervention on the offspring of overweight mothers, presenting an intriguing differential effect that requires further study.

Pre-conception, intra-uterine and early post-natal life periods are critical developmental windows that can impact on health and disease in later life. The selection of children in our study was purposeful to include those whose mothers had a good attendance at the initial PWGs that concentrated on issues such as maternal nutrition, taking rest, and shunning the habit of 'eating down' to ensure a small baby for easier delivery. Many of these women will have subsequently been exposed to further PWGs focused on improving feeding practices, hygiene and nutrition for children under five. Though data on the precise proportion of women exposed to both PWG cycles are not available, it is likely that the majority participated in both. Thus, PWGs could have impacted on all the aforementioned developmental periods, making it difficult to identify when, if at all, the PWG intervention may have had greater influence on postnatal child growth. Further, as we do not have birth weight data, we are unable to disentangle an *in-utero* effect from a postnatal effect or whether the observed differences are more likely a combination of both.

Mothers who attended the PWG interventions may have practised better hygiene, thus protecting their child from infections and improving nutritional status. Hygienic delivery practices, early initiation of breastfeeding and essential newborn care were indeed observed in our trial of the PWG impact on neonatal outcomes[9]. Furthermore, verbal autopsy data from the trial suggest that reductions in deaths due to neonatal infections may have largely contributed to impacts on neonatal mortality. Formative evaluation of the PWG intervention on post-neonatal child health in a subset of groups supports a link with improved hygiene[10]. Despite no changes in care-seeking, there were significant improvements in mothers' knowledge of disease prevention and management, including giving anthelminthics, danger signs and hand washing at critical times. Reduced maternal

reports of under-five morbidities and duration of illness were also observed[10]. Significant increases were also seen in the intervention group for both exclusive breastfeeding for at least six months, and the mean duration of breastfeeding[10]. We did not measure maternal dietary intake or energy expenditure during pregnancy, although dietary advice was a core component of the PWGs.

It is important to understand the differential effect of the intervention by maternal BMI group. Previous evidence shows that PWG interventions can address the health needs of more marginalised women and children[17]. Assuming the underweight BMI group represents more marginalised women, our findings may also reflect this phenomenon. Nevertheless, we cannot exclude the possibility that the differential effects by maternal BMI were due to underlying differences in newborn and infant care and feeding practices, or other background and socioeconomic factors between BMI groups.

Major strengths of this study are its large size, high quality fieldworker-collected anthropometric data, and high follow-up rates. However, the fact that the intervention sample included women who had actively participated in at least six PWG meetings means that this is a self-selecting group which diminishes their comparability to the randomly sampled control group. The analysis therefore compares a highly exposed and compliant intervention group with a random sample from the general unexposed community. However, given the formative, exploratory nature of this study and the need to better understand early life influences on growth, we felt it was important to target an intervention sample that had maximum feasible exposure to the intervention during their pregnancy. Indeed the socioeconomic parameters described in Table 1 do not differ

substantially in terms of common background characteristics, although we acknowledge the potential for underlying differences not measured, not least infant birth weight, and we have tried to control for a survival bias in intervention clusters by controlling for mother-child height difference. A further limitation is that our measures of maternal height and weight were recorded during this follow-up study and not during the initial intervention or pregnancy. Additional measures of sitting height/leg length as well as paternal height could also strengthen future studies.

Conclusion

Our findings imply a lasting positive effect of the PWG intervention on lean mass and frame size, and supports the need for further work evaluating the potential of community-based maternal and child health interventions to promote child growth and development and prevent cardiometabolic diseases.

List of abbreviations

BMI – Body Mass Index

PWG – Participatory Women's Groups

PLA – Participatory Learning and Action

MUAC – Mid-upper-arm circumference

WAZ – Weight-for-age z-score

WHZ – Weight-for-height z-score

HAZ – Height-for-age z-score

HC- Head circumference

CC – Chest circumference

AC – Abdominal circumference

Declarations

None.

Ethical approval

The study was approved by the Institutional Ethical Review Board of the Diabetic Association of Bangladesh (BADAS ERC/EC/13/00108). The original PWG trial was approved by the University College London research ethics committee (identification no. 1488/001). Women who chose to participate with their child in the study gave verbal consent and were free to decline an interview at any time.

Consent for Publication

Not applicable

Availability of data and materials

The datasets generated and analysed during this study are available from the corresponding author on reasonable request.

Competing Interests

None declared.

Funding

The research leading to these results has received funding from the European Union's

Seventh Framework Programme under EC-GA No. 278917 (GIFTS).

The funder played no part in the study design, data collection, analysis, interpretation of results, writing the report, or the decision to submit for publication.

Author Contributions

EF, NA, AC, KA, SF and GH developed the study protocol. EF & NA prepared the first draft of the manuscript; EF coordinated revisions and prepared the final manuscript draft. NA & SKS coordinated fieldwork and data capture activities. BNB managed data processes. TN coordinated the original participatory women's groups intervention and managed data on individual women's participation and attendance in groups. EF led statistical analysis with BNB and with technical input from CF, CGE and CO. CF contributed to anthropometric protocol development and fieldworker training. AK & KA provided overall leadership and coordination of the project in Bangladesh. KA & AC were principal investigators of the original PWG trial and, together with CF, CGE, SF, VG, AK and GH, contributed substantially to the interpretation of study findings. All authors reviewed, contributed to and approved the final manuscript.

Licence for publication

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence on a worldwide basis to the BMJ Publishing Group Ltd to permit this article to be published in JECH and any other BMJPGL products and sub-licences such use and exploit all subsidiary rights, as set out in: <u>http://group.bmj.com/products/journals/instructions-for-authors/licence-forms</u>.

References

- 1. Sudfeld CR, Charles McCoy D, Danaei G, Fink G, Ezzati M, Andrews KG, Fawzi WW: Linear Growth and Child Development in Low- and Middle-Income Countries: A Meta-Analysis. *Pediatrics* 2015, **135**(5):e1266-e1275.
- 2. Huang RC, Prescott SL, Godfrey KM, Davis EA: Assessment of cardiometabolic risk in children in population studies: underpinning developmental origins of health and disease mother-offspring cohort studies. *Journal of nutritional science* 2015, **4**:e12.
- 3. Barker DJP: Fetal origins of coronary heart disease. *British Medical Journal* 1995, **311**(6998):171-174.
- 4. Barker D, Gluckman P, Godfrey K, Harding J: **Fetal nutrition and cardiovascular disease in** adult life. *Lancet* 1993, **341**:938-941.
- 5. Christian P, Stewart C: Maternal micronutrient deficiency, fetal development, and the risk of chronic disease. *J Nutr* 2010, **140**:437–445.
- 6. Waterland R, Michels K: Epigenetic epidemiology of the developmental origins hypothesis. Annu Rev Nutr 2007, 27:363–388.
- 7. Kamal SM, Hassan CH, Alam GM: **Dual burden of underweight and overweight among women in Bangladesh: patterns, prevalence, and sociodemographic correlates**. *Journal of health, population, and nutrition* 2015, **33**(1):92-105.
- 8. Susan van D, Beulens JWJ, Yvonne T. van der S, Grobbee DE, Nealb B: **The global burden of diabetes and its complications: an emerging pandemic**. *European Journal of Cardiovascular Prevention & Rehabilitation* 2010, **17**(1 suppl):s3-s8.
- Fottrell E, Azad K, Kuddus A, Younes L, Shaha S, Nahar T, Haq Aumon B, Hossen M, Beard J, Hossain T *et al*: The effect of increased coverage of participatory women's groups on neonatal mortality in Bangladesh: a cluster randomized trial. *JAMA Pediatrics* 2013, 167(9):816-825.
- 10. Younes L, Houweling TAJ, Azad K, Kuddus A, Shaha S, Haq B, Nahar T, Hossen M, Beard J, Copas A *et al*: **The effect of participatory women's groups on infant feeding and child health knowledge, behaviour and outcomes in rural Bangladesh: a controlled before-andafter study**. *Journal of Epidemiology and Community Health* 2015, **69**:374-381.
- 11. Harris-Fry HA, Azad K, Younes L, Kuddus A, Shaha S, Nahar T, Hossen M, Costello A, Fottrell E: Formative evaluation of a participatory women's groups intervention on reproductive and women's health outcomes in rural Bangladesh: a controlled before and after study. *Journal of Epidemiology and Community Health* 2016, **0**:1-8.
- 12. Houweling TAJ, Azad K, Younes L, Kuddus A, Shaha SK, Nahar T, Beard J, Fottrell E, Prost A, Costello A: The effect of participatory women's groups on birth outcomes in Bangladesh: does coverage matter? A cluster randomised trial. *Trials* 2011, **12**(208).
- 13. Shiwaku K, Anuurad E, Enkhmaa B, Kitajima K, Yamane Y: **Appropriate BMI for Asian populations**. *Lancet* 2004, **363**(9414):1077.
- 14. Lawn JE, Osrin D, Adler A, Cousens S: Four million neonatal deaths: counting and attribution of cause of death. *Paediatric and perinatal epidemiology* 2008, **22**(5):410-416.
- 15. (NIPORT) NIOPRaT, Associates Ma, International I: **Bangladesh Demographic anf Health Survey 2014**. Dhaka, Bangladesh; 2016.
- 16. Finer S, Iqbal MS, Lowe R, Ogunkolade BW, Pervin S, Mathews C, Smart M, Alam DS, Hitman GA: Is famine exposure during developmental life in rural Bangladesh associated with a metabolic and epigenetic signature in young adulthood? A historical cohort study. *BMJ Open* 2016, **6**(11):e011768.
- 17. Houweling TAJ, Morrison J, Alcock G, Azad K, Das S, Hossen M, Kuddus A, Lewycka S, Looman CW, Magar BB *et al*: **Reaching the poor with health interventions: programme-incidence analysis of seven randomised trials of women's groups to reduce newborn mortality in Asia and Africa**. *Journal of Epidemiology and Community Health* 2016, **70**(1):31-41.

Figure 1: Regression coefficients and 95% confidence intervals showing intervention effect on child anthropometrics overall (a) and stratified by maternal BMI as underweight (BMI <18.5), overweight (BMI ≥23) or normal (BMI ≥18 but <23) (b). Results are adjusted for maternal education, household assets and mother-child height difference. *Indicates p<0.05.