Metformin in PCOS pregnancies Implications for the children

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¹Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology, Norway; ²Department of Clinical Science, University of Bergen, Norway; ³Departement of Endocrinology, Trondheim University Hospital, Norway; ⁴Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, Norway; ⁵Children's clinic, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, Trondheim University Hospital, Norway; ⁶Departement of Obstetrics and Gynecology, T

Conclusion

- Children exposed to metformin in utero had increased risk of obesity and central adiposity
- The metformin effect was more pronounced when mothers had high pre-pregnancy BMI
- Our results endorse cautious use of metformin in PCOS pregnancies

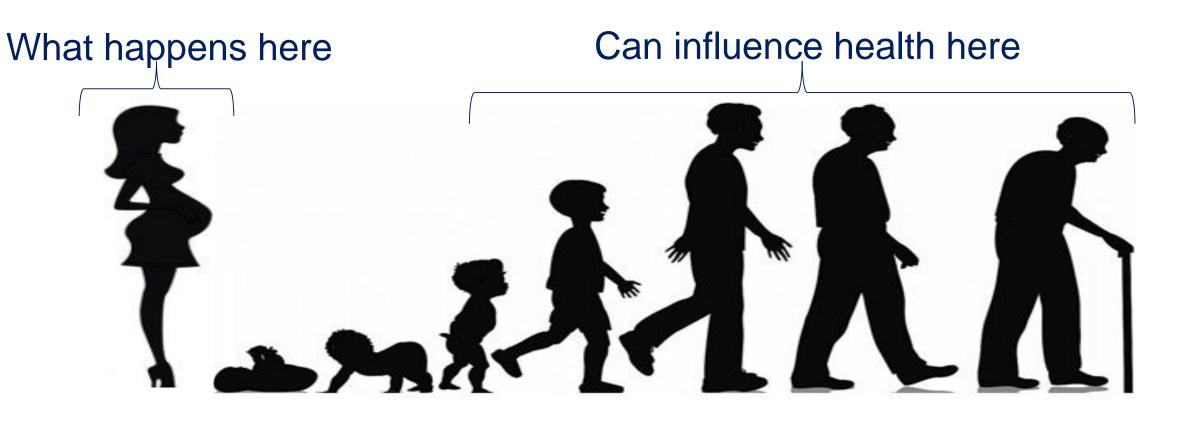
Background

Metformin is increasingly used in pregnancy; in polycystic ovary syndrome (PCOS), GDM and obesity It passes the placenta, with limited information on consequences for the offspring



Follow-up of 141 children from the PregMet-study¹, an RCT comparing metformin (2000 mg daily) to placebo during PCOS pregnancies

Aim: to explore possible effects of intrauterine metformin exposure on metabolic health, in children of women with PCOS



- Primary end-point: age-and-gender adjusted BMI
- Secondary end-points: other age-and-gender adjusted anthropometric measurements, bioimpedance measurements, BMI categories, blood lipids, fasting glucose, HbA1c and blood pressure

Anthropometric measurements were converted to z-scores^{2,3}

Results

Mean age at inclusion was 7.4 \pm 1.2 SD in the placebo group and 7.6 \pm 1.3 SD in the metformin group

Metformin exposed children had higher BMI z-score, waist-toheight ratio z-score and waist circumference z-score There was no difference in biochemical analyses or blood pressure

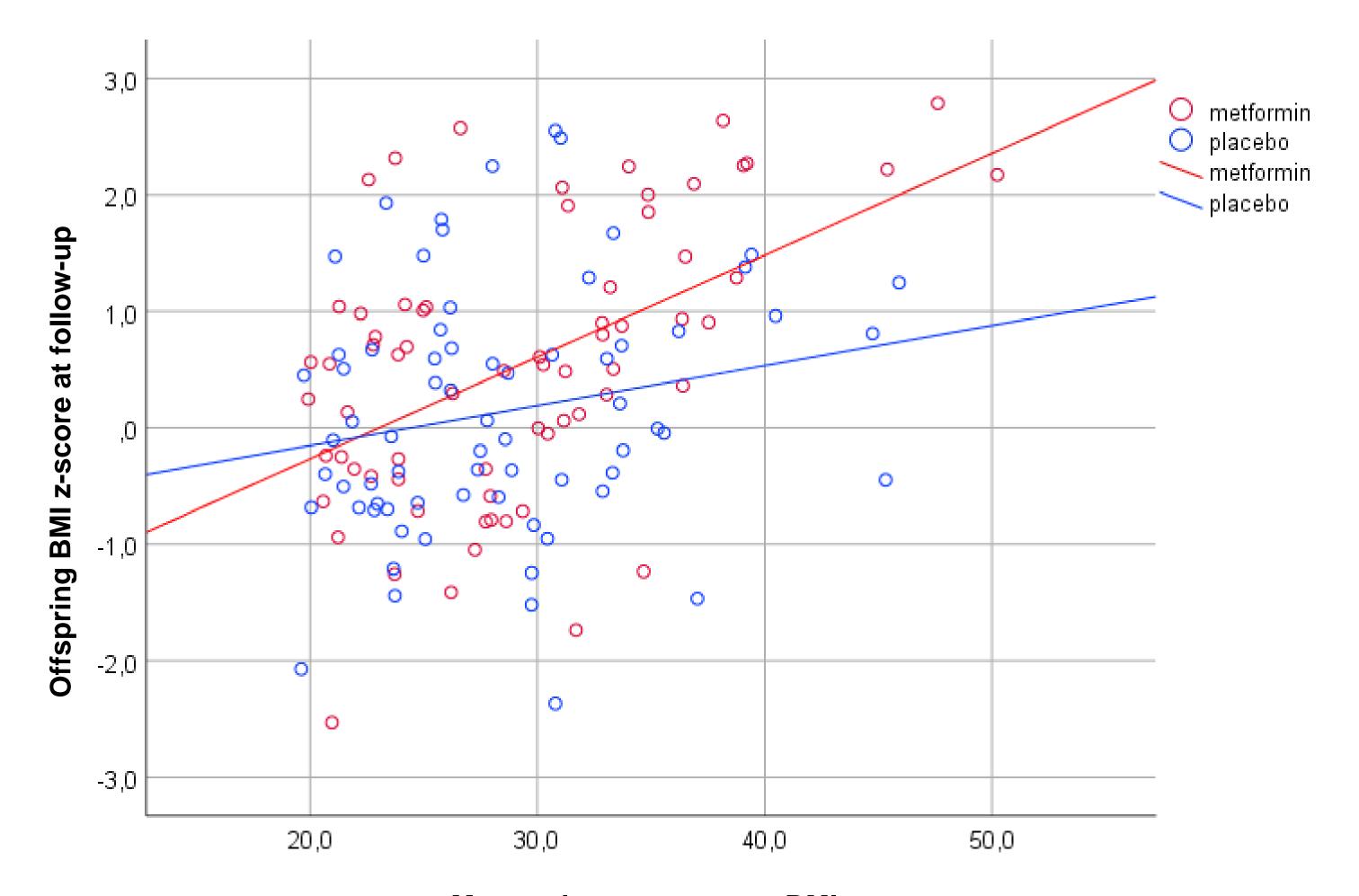
Maternal baseline characteristics	acteristics Metformin n=67 Placebo n=	
	Mean±SD	Mean±SD
Age (years)	29.5 ± 3.9	30.1 ± 4.1
BMI (kg/m²)	28.8 ± 6.8	28.5 ± 6.3
Systolic blood pressure (mmHg)	118 ± 12	118 ± 12
Fasting plasma glucose (mmol/L)	4.6 ± 0.5	4.7 ± 0.6
2 h plasma glucose (mmol/L)	5.3 ± 1.5	5.4 ± 1.7
Cholesterol (mmol/L)	4.8 ± 1.1	4.4 ± 0.7
High Density Lipoprotein (mmol/L)	1.6 ± 0.4	1.6 ± 0.3
Triglycerides (mmol/L)	1.2 ± 0.5	1.1 ± 0.5
Smoking (%)	4 (6.0)	3 (4.6)

The effect of metformin on offspring BMI z-score increased by 0.05 SD (95% CI 0.00 to 0.11, p=0.052) with every unit increase in maternal pre-pregnancy BMI

Body composition, biochemical markers and blood pressure of metformin and placebo exposed offspring

Waist-to-height ratio z-score Waist circumference z-score $0.81 (0.57-1.06)$ $0.45 (0.27-0.64)$ 0.64 Weight z-score Weight z-score $0.83 (0.59-1.08)$ $0.43 (0.23-0.64)$ $0.63 (0.23-0.64)$ $0.63 (0.23-0.64)$ $0.63 (0.23-0.28)$ $0.$	cxposed onspring	Metformin, n=69 Mean (95% CI)	Placebo, n=70 Mean (95% CI)	р
Waist-to-height ratio z-score 0.81 (0.57-1.06) 0.45 (0.27-0.64) 0 Waist circumference z-score 0.83 (0.59-1.08) 0.43 (0.23-0.64) 0 Weight z-score 0.53 (0.25-0.80) 0.10 (-0.18-0.38) 0 Height z-score 0.19 (-0.05-0.42) 0.03 (-0.23-0.28) 3 Bioelectrical impedance 11.13 (10.2-12.1) 10.50 (9.8-11.2) 2 Body fat (kg) 6.84 (5.3-8.4) 5.05 (4.2-5.9) 0 Body fat (%) 21.64 (18.9-24.4) 18.59 (16.3-20.9) 0 Biochemical analyses 0.63 (0.57-0.68) 0.60 (0.53-0.66) 4 HDL cholesterol (mmol/l) 1.59 (1.51-1.68) 1.59 (1.49-1.70) 9 Fasting glucose (mmol/l) 4.71 (4.59-4.83) 4.91 (4.54-5.28) 2 HbA1c (%) 5.06 (5.01-5.10) 5.11 (4.97-5.25) 4 Blood pressure 5 53 (75.7) 7 BMI categories n (%) 1 1 1.4 9 Underweight grade 1 1 (1.4) 1 (1.4) 9 Underweight grade 2 1 (1.4) 1 (1.4) <td>Anthropometry</td> <td></td> <td>, , , , , , , , , , , , , , , , , , ,</td> <td></td>	Anthropometry		, , , , , , , , , , , , , , , , , , ,	
Waist circumference z-score 0.83 (0.59-1.08) 0.43 (0.23-0.64) 0 Weight z-score 0.53 (0.25-0.80) 0.10 (-0.18-0.38) 0 Height z-score 0.19 (-0.05-0.42) 0.03 (-0.23-0.28) 3 Bioelectrical impedance 11.13 (10.2-12.1) 10.50 (9.8-11.2) 2 Body fat (kg) 6.84 (5.3-8.4) 5.05 (4.2-5.9) 0 Body fat (%) 21.64 (18.9-24.4) 18.59 (16.3-20.9) 0 Biochemical analyses 0.63 (0.57-0.68) 0.60 (0.53-0.66) 4 HDL cholesterol (mmol/l) 1.59 (1.51-1.68) 1.59 (1.49-1.70) 9 Fasting glucose (mmol/l) 4.71 (4.59-4.83) 4.91 (4.54-5.28) 2 HbA1c (%) 5.06 (5.01-5.10) 5.11 (4.97-5.25) 4 Blood pressure 5 53 (75.7) 7 BMI categories n (%) 1 1 1.4) 9 Underweight grade 1 1 (1.4) 1 (1.4) 9 Underweight grade 1 1 (1.4) 1 (1.4) 9 Underweight grade 1 1 (1.4) 1 (1.4) 9 <	BMI z-score	0.54 (0.26-0.83)	0.14 (-0.12-0.39)	.03
Weight z-score $0.53 (0.25-0.80)$ $0.10 (-0.18-0.38)$ $0.03 (-0.23-0.28)$ 3.3 Bioelectrical impedanceMuscle mass (kg) $11.13 (10.2-12.1)$ $10.50 (9.8-11.2)$ 2.2 Body fat (kg) $6.84 (5.3-8.4)$ $5.05 (4.2-5.9)$ 0.3 Biochemical analyses $21.64 (18.9-24.4)$ $18.59 (16.3-20.9)$ 0.3 Cholesterol (mmol/l) $4.14 (3.98-4.29)$ $4.15 (4.00-4.30)$ 9.9 Triglyceride (mmol/l) $0.63 (0.57-0.68)$ $0.60 (0.53-0.66)$ 4.4 HDL cholesterol (mmol/l) $1.59 (1.51-1.68)$ $1.59 (1.49-1.70)$ 9.9 Fasting glucose (mmol/l) $4.71 (4.59-4.83)$ $4.91 (4.54-5.28)$ 2.2 HbA1c (%) $5.06 (5.01-5.10)$ $5.11 (4.97-5.25)$ 4.4 Blood pressure $8BP (mmHg)$ $104 (102-106)$ $103 (101-105)$ 5.5 DBP (mmHg) $65 (64-67)$ $65 (63-67)$ 7.7 BMI categories n (%) $Underweight grade 2$ $1 (1.4)$ $1 (1.4)$ 9.9 Underweight grade 1 $1 (1.4)$ $2 (2.9)$ $5.3 (75.7)$ 1.4 Overweight $8 (11.6)$ $11 (15.7)$ $4.5 (65.2)$ $53 (75.7)$ $1.5 (2.9)$ Normal weight $2 (2.9)$ $2 (2.9)$ 9.9 9.9 Morbid obesity $2 (2.9)$ $2 (2.9)$ 9.9 Metabolically abnormal $5 (8.3)$ $0 (0.0)$ 0.0	Waist-to-height ratio z-score	0.81 (0.57-1.06)	0.45 (0.27-0.64)	.02
Height z-score 0.19 (-0.05-0.42) 0.03 (-0.23-0.28) .3 Bioelectrical impedance Muscle mass (kg) 11.13 (10.2-12.1) 10.50 (9.8-11.2) .2 Body fat (kg) 6.84 (5.3-8.4) 5.05 (4.2-5.9) .0 Body fat (%) 21.64 (18.9-24.4) 18.59 (16.3-20.9) .0 Biochemical analyses	Waist circumference z-score	0.83 (0.59-1.08)	0.43 (0.23-0.64)	.01
Bioelectrical impedance11.13 (10.2-12.1)10.50 (9.8-11.2)2Body fat (kg) $6.84 (5.3-8.4)$ $5.05 (4.2-5.9)$.0Body fat (%) $21.64 (18.9-24.4)$ $18.59 (16.3-20.9)$.0Biochemical analyses $Cholesterol (mmol/l)$ $4.14 (3.98-4.29)$ $4.15 (4.00-4.30)$.9Triglyceride (mmol/l) $0.63 (0.57-0.68)$ $0.60 (0.53-0.66)$.4HDL cholesterol (mmol/l) $1.59 (1.51-1.68)$ $1.59 (1.49-1.70)$.9Fasting glucose (mmol/l) $4.71 (4.59-4.83)$ $4.91 (4.54-5.28)$.2HbA1c (%) $5.06 (5.01-5.10)$ $5.11 (4.97-5.25)$.4Blood pressure $SBP (mmHg)$ $104 (102-106)$ $103 (101-105)$.5DBP (mmHg) $65 (64-67)$ $65 (63-67)$.7BMI categories n (%) $1 (1.4)$ $1 (1.4)$.9Underweight grade 2 $1 (1.4)$ $1 (1.4)$.9Underweight grade 1 $1 (1.4)$ $2 (2.9)$.5Normal weight $45 (65.2)$ $53 (75.7)$.1Overweight $8 (11.6)$ $11 (15.7)$.4Obesity $2 (2.9)$ $2 (2.9)$.9Metabolically abnormal $5 (8.3)$ $0 (0.0)$.0	Weight z-score	0.53 (0.25-0.80)	0.10 (-0.18-0.38)	.03
Muscle mass (kg) $11.13 (10.2-12.1)$ $10.50 (9.8-11.2)$ 22 Body fat (kg) $6.84 (5.3-8.4)$ $5.05 (4.2-5.9)$ 00 Body fat (%) $21.64 (18.9-24.4)$ $18.59 (16.3-20.9)$ 00 Biochemical analyses $-1.64 (18.9-24.4)$ $18.59 (16.3-20.9)$ 00 Cholesterol (mmol/l) $4.14 (3.98-4.29)$ $4.15 (4.00-4.30)$ 90 Triglyceride (mmol/l) $0.63 (0.57-0.68)$ $0.60 (0.53-0.66)$ 40 HDL cholesterol (mmol/l) $1.59 (1.51-1.68)$ $1.59 (1.49-1.70)$ 90 Fasting glucose (mmol/l) $4.71 (4.59-4.83)$ $4.91 (4.54-5.28)$ 22 HbA1c (%) $5.06 (5.01-5.10)$ $5.11 (4.97-5.25)$ 40 Blood pressure $506 (64-67)$ $65 (63-67)$ 77 BMI categories n (%) $104 (102-106)$ $103 (101-105)$ 55 Underweight grade 2 $1 (1.4)$ $1 (1.4)$ 99 Underweight grade 1 $1 (1.4)$ $2 (2.9)$ 55 Normal weight $45 (65.2)$ $53 (75.7)$ 11 Overweight $8 (11.6)$ $11 (15.7)$ 44 Obesity $2 (2.9)$ $2 (2.9)$ 99 Metabolically abnormal $5 (8.3)$ $0 (0.0)$ 00	Height z-score	0.19 (-0.05-0.42)	0.03 (-0.23-0.28)	.36
Body fat (kg) 6.84 (5.3-8.4) 5.05 (4.2-5.9) .0 Body fat (%) 21.64 (18.9-24.4) 18.59 (16.3-20.9) .0 Biochemical analyses Cholesterol (mmol/l) 4.14 (3.98-4.29) 4.15 (4.00-4.30) .9 Triglyceride (mmol/l) 0.63 (0.57-0.68) 0.60 (0.53-0.66) .4 HDL cholesterol (mmol/l) 1.59 (1.51-1.68) 1.59 (1.49-1.70) .9 Fasting glucose (mmol/l) 4.71 (4.59-4.83) 4.91 (4.54-5.28) .2 HbA1c (%) 5.06 (5.01-5.10) 5.11 (4.97-5.25) .4 Blood pressure SBP (mmHg) 104 (102-106) 103 (101-105) .5 DBP (mmHg) 65 (64-67) 65 (63-67) .7 BMI categories n (%) Underweight grade 2 1 (1.4) 1 (1.4) .9 Underweight grade 1 1 (1.4) 2 (2.9) .5 Normal weight 45 (65.2) 53 (75.7) .1 Overweight obesity 2 (2.9) 2 (2.9) .9 .9 .9 Morbid obesity 2 (2.9) 2 (2.9) .9 .9 .9 .9<	Bioelectrical impedance			
Body fat (%) 21.64 (18.9-24.4) 18.59 (16.3-20.9) .0 Biochemical analyses 4.14 (3.98-4.29) 4.15 (4.00-4.30) .9 Triglyceride (mmol/l) 0.63 (0.57-0.68) 0.60 (0.53-0.66) .4 HDL cholesterol (mmol/l) 1.59 (1.51-1.68) 1.59 (1.49-1.70) .9 Fasting glucose (mmol/l) 4.71 (4.59-4.83) 4.91 (4.54-5.28) .2 HbA1c (%) 5.06 (5.01-5.10) 5.11 (4.97-5.25) .4 Blood pressure 5.8P (mmHg) 104 (102-106) 103 (101-105) .5 DBP (mmHg) 65 (64-67) 65 (63-67) .7 BMI categories n (%) 11 (1.4) 1 (1.4) .9 Underweight grade 2 1 (1.4) 1 (1.4) .9 Underweight grade 1 1 (1.4) 2 (2.9) .5 Normal weight 45 (65.2) 53 (75.7) .1 Obesity 12 (17.4) 1 (1.4) .00 Morbid obesity 2 (2.9) .9 .9 Metabolically abnormal 5 (8.3) 0 (0.0) .0	Muscle mass (kg)	11.13 (10.2-12.1)	10.50 (9.8-11.2)	.29
Biochemical analyses 4.14 (3.98-4.29) 4.15 (4.00-4.30) .9 Triglyceride (mmol/l) 0.63 (0.57-0.68) 0.60 (0.53-0.66) .4 HDL cholesterol (mmol/l) 1.59 (1.51-1.68) 1.59 (1.49-1.70) .9 Fasting glucose (mmol/l) 4.71 (4.59-4.83) 4.91 (4.54-5.28) .2 HbA1c (%) 5.06 (5.01-5.10) 5.11 (4.97-5.25) .4 Blood pressure 5 56 (64-67) 65 (63-67) .7 BMI categories n (%) 104 (102-106) 103 (101-105) .5 Underweight grade 2 1 (1.4) 1 (1.4) .9 Underweight grade 1 1 (1.4) 2 (2.9) .5 Normal weight 45 (65.2) 53 (75.7) .1 Overweight obesity 12 (17.4) 1 (1.4) .00 Morbid obesity 2 (2.9) .9 .9 Metabolically abnormal 5 (8.3) 0 (0.0) .0	Body fat (kg)	6.84 (5.3-8.4)	5.05 (4.2-5.9)	.05
Cholesterol (mmol/l)4.14 (3.98-4.29)4.15 (4.00-4.30).9Triglyceride (mmol/l)0.63 (0.57-0.68)0.60 (0.53-0.66).4HDL cholesterol (mmol/l)1.59 (1.51-1.68)1.59 (1.49-1.70).9Fasting glucose (mmol/l)4.71 (4.59-4.83)4.91 (4.54-5.28).2HbA1c (%)5.06 (5.01-5.10)5.11 (4.97-5.25).4Blood pressureSBP (mmHg)104 (102-106)103 (101-105).5DBP (mmHg)65 (64-67)65 (63-67).7BMI categories n (%)underweight grade 21 (1.4)1 (1.4).9Underweight grade 11 (1.4)2 (2.9).5Normal weight45 (65.2)53 (75.7).1Overweight8 (11.6)11 (15.7).4Obesity2 (2.9)2 (2.9).9Metabolically abnormal5 (8.3)0 (0.0).0	Body fat (%)	21.64 (18.9-24.4)	18.59 (16.3-20.9)	.09
Triglyceride (mmol/l) $0.63 (0.57-0.68)$ $0.60 (0.53-0.66)$.4HDL cholesterol (mmol/l) $1.59 (1.51-1.68)$ $1.59 (1.49-1.70)$.9Fasting glucose (mmol/l) $4.71 (4.59-4.83)$ $4.91 (4.54-5.28)$.2HbA1c (%) $5.06 (5.01-5.10)$ $5.11 (4.97-5.25)$.4Blood pressure $104 (102-106)$ $103 (101-105)$.5DBP (mmHg) $65 (64-67)$ $65 (63-67)$.7BMI categories n (%) $1 (1.4)$ $1 (1.4)$.9Underweight grade 2 $1 (1.4)$ $1 (1.4)$.9Underweight grade 1 $1 (1.4)$ $2 (2.9)$.5Normal weight $45 (65.2)$ $53 (75.7)$.1Overweight $8 (11.6)$ $11 (15.7)$.4Obesity $2 (2.9)$ $2 (2.9)$.9Metabolically abnormal $5 (8.3)$ $0 (0.0)$.0	Biochemical analyses			
HDL cholesterol (mmol/l)1.59 (1.51-1.68)1.59 (1.49-1.70).9Fasting glucose (mmol/l)4.71 (4.59-4.83)4.91 (4.54-5.28).2HbA1c (%)5.06 (5.01-5.10)5.11 (4.97-5.25).4Blood pressureSBP (mmHg)104 (102-106)103 (101-105).5DBP (mmHg)65 (64-67)65 (63-67).7BMI categories n (%)Underweight grade 21 (1.4)1 (1.4).9Underweight grade 11 (1.4)2 (2.9).5Normal weight45 (65.2)53 (75.7).1Overweight8 (11.6)11 (15.7).4Obesity12 (17.4)1 (1.4).00Morbid obesity2 (2.9).5.9Metabolically abnormal5 (8.3)0 (0.0).0	Cholesterol (mmol/l)	4.14 (3.98-4.29)	4.15 (4.00-4.30)	.91
Fasting glucose (mmol/l)4.71 (4.59-4.83)4.91 (4.54-5.28).2HbA1c (%)5.06 (5.01-5.10)5.11 (4.97-5.25).4Blood pressure5BP (mmHg)104 (102-106)103 (101-105).5DBP (mmHg)65 (64-67)65 (63-67).7BMI categories n (%)Underweight grade 21 (1.4)1 (1.4).9Underweight grade 11 (1.4)2 (2.9).5Normal weight45 (65.2)53 (75.7).1Overweight8 (11.6)11 (15.7).4Obesity12 (17.4)1 (1.4).00Morbid obesity2 (2.9).5.9Metabolically abnormal5 (8.3)0 (0.0).0	Triglyceride (mmol/l)	0.63 (0.57-0.68)	0.60 (0.53-0.66)	.45
HbA1c (%)5.06 (5.01-5.10)5.11 (4.97-5.25).4Blood pressureSBP (mmHg)104 (102-106)103 (101-105).5DBP (mmHg)65 (64-67)65 (63-67).7BMI categories n (%)Underweight grade 21 (1.4)1 (1.4).9Underweight grade 11 (1.4)2 (2.9).5Normal weight45 (65.2)53 (75.7).1Overweight8 (11.6)11 (15.7).4Obesity12 (17.4)1 (1.4).00Morbid obesity2 (2.9).9.9Metabolically abnormal5 (8.3)0 (0.0).0	HDL cholesterol (mmol/l)	1.59 (1.51-1.68)	1.59 (1.49-1.70)	.97
Blood pressure SBP (mmHg) 104 (102-106) 103 (101-105) .5 DBP (mmHg) 65 (64-67) 65 (63-67) .7 BMI categories n (%) 1 (1.4) 1 (1.4) .9 Underweight grade 2 1 (1.4) 1 (1.4) .9 Underweight grade 1 1 (1.4) 2 (2.9) .5 Normal weight 45 (65.2) 53 (75.7) .1 Overweight 8 (11.6) 11 (15.7) .4 Obesity 12 (17.4) 1 (1.4) .00 Morbid obesity 2 (2.9) .9 .9 Metabolically abnormal 5 (8.3) 0 (0.0) .0	Fasting glucose (mmol/l)	4.71 (4.59-4.83)	4.91 (4.54-5.28)	.29
SBP (mmHg) 104 (102-106) 103 (101-105) .5 DBP (mmHg) 65 (64-67) 65 (63-67) .7 BMI categories n (%) 1 (1.4) 1 (1.4) .9 Underweight grade 2 1 (1.4) 1 (1.4) .9 Underweight grade 1 1 (1.4) 2 (2.9) .5 Normal weight 45 (65.2) 53 (75.7) .1 Overweight 8 (11.6) 11 (15.7) .4 Obesity 12 (17.4) 1 (1.4) .00 Morbid obesity 2 (2.9) .9 .0 Metabolically abnormal 5 (8.3) 0 (0.0) .0	HbA1c (%)	5.06 (5.01-5.10)	5.11 (4.97-5.25)	.42
DBP (mmHg) 65 (64-67) 65 (63-67) .7 BMI categories n (%) 1 (1.4) 1 (1.4) .9 Underweight grade 2 1 (1.4) 2 (2.9) .5 Normal weight 45 (65.2) 53 (75.7) .1 Overweight 8 (11.6) 11 (15.7) .4 Obesity 12 (17.4) 1 (1.4) .00 Morbid obesity 2 (2.9) .9 .0 Metabolically abnormal 5 (8.3) 0 (0.0) .0	Blood pressure			
BMI categories n (%) 1 (1.4) 1 (1.4) .9 Underweight grade 2 1 (1.4) 2 (2.9) .5 Underweight grade 1 1 (1.4) 2 (2.9) .5 Normal weight 45 (65.2) 53 (75.7) .1 Overweight 8 (11.6) 11 (15.7) .4 Obesity 12 (17.4) 1 (1.4) .00 Morbid obesity 2 (2.9) .9 .9 Metabolically abnormal 5 (8.3) 0 (0.0) .0	SBP (mmHg)	104 (102-106)	103 (101-105)	.51
Underweight grade 21 (1.4)1 (1.4).9Underweight grade 11 (1.4)2 (2.9).5Normal weight45 (65.2)53 (75.7).1Overweight8 (11.6)11 (15.7).4Obesity12 (17.4)1 (1.4).00Morbid obesity2 (2.9)2 (2.9).9Metabolically abnormal5 (8.3)0 (0.0).0	DBP (mmHg)	65 (64-67)	65 (63-67)	.76
Underweight grade 1 1 (1.4) 2 (2.9) .5 Normal weight 45 (65.2) 53 (75.7) .1 Overweight 8 (11.6) 11 (15.7) .4 Obesity 12 (17.4) 1 (1.4) .00 Morbid obesity 2 (2.9) .5 Metabolically abnormal 5 (8.3) 0 (0.0) .0	BMI categories n (%)			
Normal weight 45 (65.2) 53 (75.7) .1 Overweight 8 (11.6) 11 (15.7) .4 Obesity 12 (17.4) 1 (1.4) .00 Morbid obesity 2 (2.9) 2 (2.9) .9 Metabolically abnormal 5 (8.3) 0 (0.0) .0	Underweight grade 2	1 (1.4)	1 (1.4)	.99
Overweight 8 (11.6) 11 (15.7) .4 Obesity 12 (17.4) 1 (1.4) .00 Morbid obesity 2 (2.9) 2 (2.9) .9 Metabolically abnormal 5 (8.3) 0 (0.0) .0	Underweight grade 1	1 (1.4)	2 (2.9)	.57
Obesity 12 (17.4) 1 (1.4) .00 Morbid obesity 2 (2.9) 2 (2.9) .9 Metabolically abnormal 5 (8.3) 0 (0.0) .0	Normal weight	45 (65.2)	53 (75.7)	.17
Morbid obesity 2 (2.9) 2 (2.9) .9 Metabolically abnormal 5 (8.3) 0 (0.0) .0	Overweight	8 (11.6)	11 (15.7)	.48
Metabolically abnormal 5 (8.3) 0 (0.0) .0	Obesity	12 (17.4)	1 (1.4)	.001
	Morbid obesity	2 (2.9)	2 (2.9)	.99
overweigh/obese n (%)	Metabolically abnormal overweigh/obese n (%)	5 (8.3)	0 (0.0)	.06

No difference (p-value < 0.05) between the groups, except cholesterol (p=0.009)



Maternal pre-pregnancy BMI Scatterplot on the association between maternal pre-pregnancy BMI and offspring BMI z-score at follow-up

¹Vanky E, et.al. Metformin versus placebo from first trimester to delivery in polycystic ovary syndrome: a randomized, controlled multicenter study. *J Clin Endocrinol Metab.* 2010;95(12):E448-455 ²Juliusson PB et.al. Growth references for 0-19 year-old Norwegian children for length/height, weight, body mass index and head circumference. *Ann Hum Biol.* 2013;40(3):220-227 ³Brannsether B, Roelants M, Bjerknes R, Juliusson P. Waist circumference and waist-to-height ratio in Norwegian children 4–18 years of age: reference values and cut-off levels. Acta Paediatr 2011;100.

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