Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: The HAPO Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991-2002.

Table A. Additional Characteristics and Details of Outcomes of HAPO Participants

Maternal Characteristics	**N**	**Mean**	**SD**	**Range Among Centers (Mean Values)**
Education (yrs)	21,321	13.0	3.4	10.1 – 17.5
Newborn Characteristics	**N**	**Mean**	**SD**	**Range Among Centers (Mean Values)**
Length (cms)	22,601	49.7	2.4	48.7 – 50.9
Head Circumference (cms)	22,974	34.2	1.6	33.5 – 35.0
Obstetric Outcomes	**N**	**%**		**Range Among Centers (%)**
Type of Delivery				
Unassisted Vaginal	15,756	67.6		54.6 – 84.4
Vaginal Instrumental	1,997	8.6		1.9 – 14.4
Breech	40	0.2		
Primary Cesarean Section	3,731	16.0		8.6 – 23.5
Repeat Cesarean Section	1,792	7.7		3.3 – 11.8
Newborn Outcomes	**N**	**%**		**Range Among Centers (%)**
Shoulder Dystocia and/or Birth Injury	311	1.3		0.1 – 3.4
Shoulder Dystocia only	172	0.7		
Birth Injury only	99	0.4		
Shoulder Dystocia + Birth Injury	40	0.2		

Table B. Relationship between maternal glucose and birthweight > 90th percentile*.

FPG (mg/dL)	N	#	%	Model I OR	95% CI	Model II OR	95% CI
< 75	4,035	213	5.3	1.00		1.00	
75 - 79	7,501	572	7.6	1.48	(1.26 – 1.74)	1.37	(1.16 – 1.62)
80 - 84	6,168	622	10.1	2.01	(1.71 – 2.36)	1.72	(1.46 – 2.03)
85 - 89	2,741	323	11.8	2.40	(2.00 – 2.87)	1.95	(1.62 – 2.35)
90 - 94	1,883	310	16.5	3.54	(2.94 – 4.25)	2.73	(2.25 – 3.31)
95 - 99	672	124	18.5	4.06	(3.20 – 5.16)	3.00	(2.34 – 3.86)
>= 100	217	57	26.3	6.39	(4.58 – 8.91)	5.01	(3.54 – 7.09)
1-hr PG (mg/dL)	**N**	**#**	**%**	**Model I OR**	**95% CI**	**Model II OR**	**95% CI**
≤ 105	4,177	268	6.4	1.00		1.00	
106 - 132	7,524	584	7.8	1.23	(1.06 – 1.43)	1.21	(1.04 – 1.41)
133 – 155	6,003	593	9.9	1.60	(1.38 – 1.86)	1.65	(1.41 – 1.93)
156 – 171	2,768	352	12.7	2.13	(1.80 – 2.51)	2.27	(1.91 – 2.71)
172 – 193	1,858	264	14.2	2.42	(2.02 – 2.89)	2.66	(2.19 – 3.21)
194 – 211	645	111	17.2	3.03	(2.39 – 3.85)	3.50	(2.72 – 4.50)
>= 212	242	49	20.2	3.70	(2.64 – 5.19)	4.49	(3.16 – 6.39)
2-hr PG (mg/dL)	**N**	**#**	**%**	**Model I OR**	**95% CI**	**Model II OR**	**95% CI**
≤ 90	4,264	297	7.0	1.00		1.00	
91 – 108	7,422	587	7.9	1.15	(0.99 – 1.33)	1.11	(0.96 – 1.30)
109 – 125	5,865	580	9.9	1.47	(1.27 – 1.70)	1.51	(1.30 – 1.75)
126 – 139	3,024	396	13.1	2.01	(1.72 – 2.36)	2.15	(1.82 – 2.54)
140 – 157	1,720	210	12.2	1.86	(1.54 – 2.24)	2.10	(1.73 – 2.56)
158 – 177	690	101	14.6	2.29	(1.80 – 2.92)	2.68	(2.08 – 3.45)
>= 178	232	50	21.6	3.67	(2.63 – 5.13)	4.46	(3.15 – 6.33)

*Birthweight > 90th percentile: 90th percentiles for gestational age (30-44 weeks only) were determined using quantile regression analyses for each of 8 newborn gender-ethnic groups (Caucasian or Other, Black, Hispanic, Asian), with adjustment for gestational age, field center, and parity (0, 1, 2+). A newborn was considered to have a birthweight > 90th percentile if the birthweight was greater than the estimated 90th percentile for the baby's sex, gestational age, ethnicity, field center, and maternal parity. Otherwise, the newborn was considered to have a birthweight ≤ 90th percentile.

Model I: Adjusted for variables used in estimating 90th percentiles

Model II: Additional adjustment for age, BMI, BMI^2, height, smoking, alcohol use, hospitalization prior to delivery, any family history of diabetes, mean arterial blood pressure, gestational age at

OGTT N = total number in the glucose category (excluding births with gestational age < 30 weeks and fetal deaths), # = number in the glucose category with the outcome, % = proportion in the glucose category with the outcome

Table C. Relationship between maternal glucose and primary cesarean section[1].

FPG (mg/dL)	N	#	%	Model I OR	95% CI	Model II OR	95% CI
< 75	3,721	495	13.3	1.00		1.00	
75 - 79	6,806	1,151	16.9	1.30	(1.16 – 1.46)	1.19	(1.06 – 1.34)
80 - 84	5,483	1,014	18.5	1.46	(1.30 – 1.65)	1.21	(1.07 – 1.37)
85 - 89	2,378	506	21.3	1.76	(1.53 – 2.03)	1.33	(1.15 – 1.54)
90 - 94	1,601	380	23.7	2.08	(1.78 – 2.42)	1.44	(1.23 – 1.69)
95 - 99	560	134	23.9	2.17	(1.74 – 2.71)	1.39	(1.11 – 1.75)
>= 100	183	51	27.9	2.73	(1.94 – 3.85)	1.60	(1.12 – 2.27)
1-hr PG (mg/dL)	**N**	**#**	**%**	**Model I OR**	**95% CI**	**Model II OR**	**95% CI**
≤ 105	3,826	458	12.0	1.00		1.00	
106 - 132	6,792	1,113	16.4	1.36	(1.21 – 1.53)	1.21	(1.07 – 1.36)
133 – 155	5,311	1,032	19.4	1.60	(1.41 – 1.80)	1.26	(1.11 – 1.42)
156 – 171	2,425	522	21.5	1.77	(1.54 – 2.04)	1.31	(1.13 – 1.52)
172 – 193	1,623	407	25.1	2.16	(1.85 – 2.51)	1.48	(1.26 – 1.74)
194 – 211	547	132	24.1	2.02	(1.61 – 2.52)	1.30	(1.04 – 1.64)
>= 212	208	67	32.2	2.97	(2.18 – 4.06)	1.86	(1.35 – 2.57)
2-hr PG (mg/dL)	**N**	**#**	**%**	**Model I OR**	**95% CI**	**Model II OR**	**95% CI**
≤ 90	3,903	535	13.7	1.00		1.00	
91 – 108	6,664	1,032	15.5	1.09	(0.97 – 1.22)	0.97	(0.86 – 1.09)
109 – 125	5,201	1,017	19.6	1.39	(1.24 – 1.56)	1.11	(0.99 – 1.26)
126 – 139	2,650	583	22.0	1.58	(1.38 – 1.80)	1.15	(1.00 – 1.32)
140 – 157	1,506	350	23.2	1.67	(1.43 – 1.95)	1.17	(0.99 – 1.37)
158 – 177	615	162	26.3	2.00	(1.63 – 2.45)	1.32	(1.06 – 1.63)
>= 178	193	52	26.9	2.10	(1.50 – 2.93)	1.28	(0.91 – 1.81)

Model I: Adjusted for field center

Model II: Adjusted for field center, age, BMI, BMI^2, height, smoking, alcohol use, hospitalization prior to delivery, any family history of diabetes, mean arterial blood pressure, gestational age at OGTT, baby's sex

N = total number in the glucose category, # = number in the glucose category with the outcome, % = proportion in the glucose category with the outcome

[1]Excluding those with a prior cesarean section.

Table D. Relationship between maternal glucose and clinical neonatal hypoglycemia*.

FPG (mg/dL)	N	#	%	Model I OR	95% CI	Model II OR	95% CI
< 75	4,043	83	2.1	1.00		1.00	
75 - 79	7,503	144	1.9	0.97	(0.74 – 1.28)	0.91	(0.69 – 1.21)
80 - 84	6,164	122	2.0	1.04	(0.78 – 1.38)	0.92	(0.68 – 1.23)
85 - 89	2,744	59	2.2	1.19	(0.84 – 1.69)	1.00	(0.70 – 1.43)
90 - 94	1,884	48	2.5	1.51	(1.05 – 2.19)	1.19	(0.81 – 1.75)
95 - 99	672	14	2.1	1.34	(0.75 – 2.39)	1.01	(0.55 – 1.84)
>= 100	217	10	4.6	2.69	(1.35 – 5.35)	1.98	(0.97 – 4.05)
1-hr PG (mg/dL)	**N**	**#**	**%**	**Model I OR**	**95% CI**	**Model II OR**	**95% CI**
≤ 105	4,183	72	1.7	1.00		1.00	
106 - 132	7,523	153	2.0	1.21	(0.91 – 1.61)	1.12	(0.84 – 1.49)
133 – 155	6,003	131	2.2	1.44	(1.08 – 1.94)	1.24	(0.92 – 1.68)
156 – 171	2,772	54	1.9	1.37	(0.96 – 1.98)	1.11	(0.77 – 1.62)
172 – 193	1,860	45	2.4	1.96	(1.33 – 2.88)	1.48	(0.99 – 2.22)
194 – 211	643	20	3.1	2.85	(1.70 – 4.77)	2.17	(1.28 – 3.69)
>= 212	243	5	2.1	1.71	(0.68 – 4.33)	1.29	(0.51 – 3.31)
2-hr PG (mg/dL)	**N**	**#**	**%**	**Model I OR**	**95% CI**	**Model II OR**	**95% CI**
≤ 90	4,266	78	1.8	1.00		1.00	
91 – 108	7,421	134	1.8	0.92	(0.69 – 1.22)	0.87	(0.66 – 1.17)
109 – 125	5,868	117	2.0	1.08	(0.80 – 1.45)	0.96	(0.71 – 1.30)
126 – 139	3,027	80	2.6	1.47	(1.06 – 2.02)	1.23	(0.88 – 1.71)
140 – 157	1,720	44	2.6	1.43	(0.98 – 2.10)	1.13	(0.76 – 1.68)
158 – 177	693	21	3.0	1.82	(1.11 - 3.00)	1.36	(0.81 – 2.28)
>= 178	232	6	2.6	1.54	(0.66 – 3.62)	1.12	(0.47 – 2.67)

*Clinical neonatal hypoglycemia: Clinical neonatal hypoglycemia was defined as present if there was notation of neonatal hypoglycemia in the medical record and there were symptoms and/or treatment with a glucose infusion or a local laboratory report of a glucose value ≤ 30.6 mg/dL (1.7 mmol/L) in the first 24 hours and/or ≤ 45 mg/dL (2.5 mmol/L) after the first 24 hours after birth.

Model I: Adjusted for field center

Model II: Adjusted for field center, age, BMI, height, parity, smoking, alcohol use, hospitalization prior to delivery, any family history of diabetes, mean arterial blood pressure, mean arterial blood pressure squared, gestational age at OGTT, baby's sex

N = total number in the glucose category (excluding fetal deaths), # = number in the glucose category with the outcome, % = proportion in the glucose category with the outcome

Table E. Relationship between maternal glucose and cord C-peptide > 90th percentile*.

FPG (mg/dL)	N	#	%	Model I OR	95% CI	Model II OR	95% CI
< 75	3,546	131	3.7	1.00		1.00	
75 - 79	6,453	378	5.9	1.62	(1.32 – 1.98)	1.41	(1.15 – 1.74)
80 - 84	5,255	429	8.2	2.31	(1.88 – 2.83)	1.75	(1.42 – 2.15)
85 - 89	2,308	266	11.5	3.33	(2.67 – 4.15)	2.36	(1.88 – 2.97)
90 - 94	1,592	281	17.7	5.58	(4.47 – 6.96)	3.62	(2.87 – 4.58)
95 - 99	561	131	23.4	7.85	(6.00 – 10.26)	4.46	(3.36 – 5.93)
>= 100	170	55	32.4	12.42	(8.57 – 18.01)	7.65	(5.17 – 11.32)
1-hr PG (mg/dL)	**N**	**#**	**%**	**Model I OR**	**95% CI**	**Model II OR**	**95% CI**
≤ 105	3,593	176	4.9	1.00		1.00	
106 - 132	6,372	366	5.7	1.21	(1.01 – 1.46)	1.07	(0.88 – 1.29)
133 – 155	5,132	458	8.9	2.02	(1.69 – 2.43)	1.62	(1.34 – 1.95)
156 – 171	2,424	274	11.3	2.68	(2.19 – 3.27)	1.95	(1.58 – 2.41)
172 – 193	1,607	251	15.6	3.88	(3.16 – 4.78)	2.76	(2.21 – 3.43)
194 – 211	549	95	17.3	4.49	(3.41 – 5.90)	2.91	(2.18 – 3.89)
>= 212	208	51	24.5	6.94	(4.85 – 9.91)	4.65	(3.19 – 6.79)
2-hr PG (mg/dL)	**N**	**#**	**%**	**Model I OR**	**95% CI**	**Model II OR**	**95% CI**
≤ 90	3,599	193	5.4	1.00		1.00	
91 – 108	6,353	401	6.3	1.21	(1.02 – 1.45)	1.06	(0.88 – 1.27)
109 – 125	5,039	440	8.7	1.79	(1.50 – 2.14)	1.44	(1.20 – 1.73)
126 – 139	2,609	286	11.0	2.37	(1.95 – 2.88)	1.72	(1.40 – 2.11)
140 – 157	1,495	202	13.5	3.00	(2.43 – 3.71)	2.21	(1.77 – 2.76)
158 – 177	596	109	18.3	4.35	(3.36 – 5.63)	2.86	(2.18 – 3.77)
>= 178	194	40	20.6	5.09	(3.48 – 7.47)	3.48	(2.33 – 5.21)

*Cord C-peptide > 90th percentile: Defined from the total HAPO sample with a C-peptide result

Model I: Adjusted for field center

Model II: Adjusted for field center, age, BMI, BMI^2, height, parity, smoking, alcohol use, hospitalization prior to delivery, any family history of diabetes, mean arterial blood pressure (MAP), MAP^2, gestational age at OGTT, and cord glucose (excluding 200 women who were missing the cord glucose), baby's sex

N = total number in the glucose category (excluding fetal deaths), # = number in the glucose category with the outcome, % = proportion in the glucose category with the outcome

Table F. Relationship* between maternal glucose and primary and secondary perinatal outcomes.

Outcome	Model I OR	95% CI	Model II OR	95% CI
a. Primary Outcomes				
Birthweight > 90th %ile				
FPG	1.49	(1.43 – 1.55)	1.38	(1.32 – 1.44)
1-hr PG	1.39	(1.33 – 1.45)	1.46	(1.39 – 1.53)
2-hr PG	1.31	(1.25 – 1.36)	1.38	(1.32 – 1.44)
Primary cesarean section				
FPG	1.26	(1.21 – 1.30)	1.11	(1.06 – 1.15)
1-hr PG	1.25	(1.21 – 1.30)	1.10	(1.06 – 1.15)
2-hr PG	1.21	(1.17 – 1.26)	1.08	(1.03 -1.12)
Clinical neonatal hypoglycemia				
FPG	1.17**	(1.06 – 1.28)	1.08**	(0.98 – 1.19)
1-hr PG	1.24	(1.13 – 1.36)	1.13	(1.03 – 1.26)
2-hr PG	1.19	(1.09 – 1.31)	1.10	(1.00 – 1.12)
Cord C-peptide > 90th %ile				
FPG	1.77	(1.69 – 1.86)	1.55	(1.47 – 1.64)
1-hr PG	1.63	(1.55 – 1.71)	1.46	(1.38 – 1.54)
2-hr PG	1.51	(1.44 – 1.59)	1.37	(1.30 – 1.44)
b. Secondary Outcomes				
Premature delivery (< 37 wks)				
FPG	1.08***	(1.02 – 1.14)	1.05	(0.99 – 1.11)
1-hr PG	1.21	(1.15 – 1.27)	1.18	(1.12 – 1.25)
2-hr PG	1.20	(1.14 – 1.26)	1.16	(1.10 – 1.23)
Shoulder dystocia and/or birth injury				
FPG	1.19	(1.06 – 1.33)	1.18	(1.04 – 1.33)
1-hr PG	1.22	(1.09 – 1.36)	1.23	(1.09 – 1.38)
2-hr PG	1.20	(1.08 – 1.34)	1.22	(1.09 – 1.37)
Intensive neonatal care				
FPG	1.07	(1.02 – 1.13)	0.99	(0.94 – 1.05)
1-hr PG	1.14	(1.09 – 1.20)	1.07	(1.02 – 1.13)
2-hr PG	1.15	(1.10 – 1.21)	1.09	(1.03 – 1.14)
Hyperbilirubinemia				
FPG	1.06	(1.01 – 1.11)	1.00	(0.95 – 1.05)
1-hr PG	1.16	(1.10 – 1.21)	1.11	(1.05 – 1.17)

2-hr PG	1.12	(1.07 – 1.18)	1.08	(1.02 – 1.13)
Pre-eclampsia				
FPG	1.47	(1.39 – 1.56)	1.21	(1.13 – 1.29)
1-hr PG	1.39	(1.30 – 1.47)	1.28	(1.20 – 1.37)
2-hr PG	1.36	(1.28 – 1.44)	1.28	(1.20 – 1.37)

*Continuous variable analysis, glucose higher by 1 standard deviation (6.9 mg/dL for FPG, 30.9 mg/dL for 1-hr PG, 23.5 mg/dL for 2-hr PG) (mmol/L = mg/dL/18)

Model I: Adjusted for field center. Models for birthweight were adjusted for variables used in estimating 90^{th} %iles (Table B).

Model II: All models were adjusted for field center, age, BMI, height, smoking, alcohol use, family history of diabetes, gestational age at OGTT, baby's sex, parity (not included in model for primary cesarean delivery), hospitalization prior to delivery (not included in model for pre-eclampsia), mean arterial blood pressure (not included in model for pre-eclampsia). Cord glucose was included in the model for C-peptide > 90^{th} %ile, and family history of hypertension and prenatal UTI were included in the model for pre-eclampsia.