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Supplemental Material

Association of Lifetime Exposure to Glyphosate and Aminomethylphosphonic Acid (AMPA) with Liver Inflammation and Metabolic Syndrome at Young Adulthood: Findings from the CHAMACOS Study

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Table S7. Adjusted RRs and 95% CI for two-fold increases in child urinary glyphosate, AMPA, and glyphosate residue concentrations (specific gravity-corrected, μg/L) at 18 years and abnormal markers of liver inflammation and metabolic syndrome (and its components) in CHAMACOS young adults in case-control group (n=120-121).

Table S8. Adjusted RRs and 95% CI for two-fold increases in child urinary glyphosate, AMPA, and glyphosate residue concentrations (specific gravity-corrected, μg/L) and abnormal liver enzymes and metabolic syndrome (and its components) in CHAMACOS young adults in the case-control group, excluding those cases with actin smooth muscle antibody or ceruloplasmin outside of normal limits, or who reported binge drinking in the past 30 days.

Table S9. Overall p-values for visit X exposure interaction terms in multiple informant models for repeated child urinary glyphosate, AMPA, and glyphosate residue concentrations (specific gravity-corrected, μg/L) at the 5-year, 14-year, and 18-year visits and abnormal markers of liver inflammation and metabolic syndrome (and its components), using mixed-effects Poisson models with a random intercept for each CHAMACOS participant.

Table S10. Mediation analysis of child body mass (at age 14 years) on the adjusted associations (RR and 95% CI) for two-fold increases in child (ages 14 and 18 years) urinary concentrations (specific gravity-corrected) of **A.** AMPA and **B.** glyphosate residues and abnormal liver enzymes and metabolic syndrome (and its components) in CHAMACOS young adult cases and controls.

Table S11. Unadjusted RRs and 95% CI for living within 1-km of agricultural glyphosate use during maternal pregnancy (any use) and from birth to age 5 years (all use, kg, $\log_2$) based on Pesticide Use Reporting data and abnormal liver enzymes or metabolic syndrome (and its components) among all CHAMACOS young adult participants and in the case-control subset.

Figure S1. Flow diagram of participants from the CHAMACOS study.

Figure S2. Directed Acyclic Graph of the relationship between urinary glyphosate and AMPA concentrations and risk of elevated liver transaminases and metabolic syndrome (and its components).

Supplemental Material. Certificates of INSPQ's participation in the Quebec External Quality Assessment Scheme for Organic Substances in Urine (OSEQAS), German External Quality Assessment Scheme (G-EQUAS), and Human Biomonitoring for Europe (HBM4EU, reference laboratory) program.

Supplemental Table 1. Wet-weight, specific gravity-corrected, and creatinine-adjusted urinary glyphosate and AMPA concentrations in maternal urine at 26-weeks' gestation and child urine at 5-, 14-, and 18-year visits, CHAMACOS study participants.[a]

GLYPHOSATE
Wet-weight (µg/L)

Visit	n	% detected	GM (GSD)	Min	10%	25%	50%	75%	90%	Max
Full sample										
26 weeks	71	4.2%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.20
5 years	88	35.2%	<LOD	<LOD	<LOD	<LOD	<LOD	0.10	0.30	2.70
14 years	104	78.9%	0.18 (2.79)	<LOD	<LOD	0.09	0.20	0.38	0.62	1.90
18 years	121	54.6%	0.10 (3.22)	<LOD	<LOD	<LOD	0.10	0.20	0.40	6.40
Fasting	48	37.5%	<LOD	<LOD	<LOD	<LOD	<LOD	0.10	0.32	2.20
Non-fasting	73	65.8%	0.12 (3.30)	<LOD	<LOD	<LOD	0.10	0.20	0.45	6.40
Cases only										
26 weeks	26	3.9%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.20
5 years	32	46.9%	<LOD	<LOD	<LOD	<LOD	<LOD	0.10	0.30	2.70
14 years	46	76.1%	0.18 (2.92)	<LOD	<LOD	0.09	0.20	0.42	0.71	0.97
18 years	60	58.3%	0.10 (3.93)	<LOD	<LOD	<LOD	0.10	0.20	0.48	6.40
Fasting	23	39.1%	<LOD	<LOD	<LOD	<LOD	<LOD	0.10	0.32	2.20
Non-fasting	37	70.3%	0.14 (4.11)	<LOD	<LOD	<LOD	0.10	0.32	0.92	6.40
Controls only										
26 weeks	45	4.4%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.20
5 years	56	28.6%	<LOD	<LOD	<LOD	<LOD	<LOD	0.10	0.30	0.86
14 years	58	81.0%	0.18 (2.71)	<LOD	<LOD	0.10	0.20	0.35	0.54	1.90
18 years	61	50.8%	0.09 (2.56)	<LOD	<LOD	<LOD	0.08	0.20	0.32	0.92
Fasting	25	36.0%	<LOD	<LOD	<LOD	<LOD	<LOD	0.10	0.32	0.92
Non-fasting	36	61.1%	0.11 (2.51)	<LOD	<LOD	<LOD	0.10	0.20	0.40	0.65

Specific gravity-corrected (µg/L)

Visit	n	% detected	GM (GSD)	Min	10%	25%	50%	75%	90%	Max
Full sample										
26 weeks	71	4.2%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.62
5 years	88	35.2%	<LOD	<LOD	<LOD	<LOD	<LOD	0.16	0.41	4.32
14 years	104	78.9%	0.28 (2.37)	<LOD	<LOD	0.17	0.31	0.51	0.78	1.47
18 years	121	54.6%	0.16 (2.77)	<LOD	<LOD	<LOD	0.14	0.31	0.48	5.91
Fasting	48	37.5%	<LOD	<LOD	<LOD	<LOD	<LOD	0.31	0.63	2.20
Non-fasting	73	65.8%	0.17 (2.80)	<LOD	<LOD	<LOD	0.16	0.31	0.46	5.91
Cases only										
26 weeks	26	3.9%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.57
5 years	32	46.9%	<LOD	<LOD	<LOD	<LOD	<LOD	0.15	0.36	4.32
14 years	46	76.1%	0.30 (2.43)	<LOD	<LOD	0.17	0.36	0.56	0.78	1.36
18 years	60	58.3%	0.16 (3.24)	<LOD	<LOD	<LOD	0.14	0.29	0.55	5.91
Fasting	23	39.1%	<LOD	<LOD	<LOD	<LOD	<LOD	0.22	0.47	2.20
Non-fasting	37	70.3%	0.18 (3.42)	<LOD	<LOD	<LOD	0.16	0.31	0.46	5.91
Controls only										
26 weeks	45	4.4%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.62
5 years	56	28.6%	<LOD	<LOD	<LOD	<LOD	<LOD	0.17	0.44	2.78
14 years	58	81.0%	0.27 (2.34)	<LOD	<LOD	0.18	0.30	0.48	0.80	1.47
18 years	61	50.8%	0.16 (2.33)	<LOD	<LOD	<LOD	0.15	0.32	0.48	1.16
Fasting	25	36.0%	<LOD	<LOD	<LOD	<LOD	<LOD	0.33	0.65	1.16
Non-fasting	36	61.1%	0.16 (2.19)	<LOD	<LOD	<LOD	0.16	0.29	0.46	0.62

Creatinine-adjusted (µg/g creatinine)

Visit	n	% detected	GM (GSD)	Min	10%	25%	50%	75%	90%	Max
Full sample										
26 weeks	71	4.2%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	1.47
5 years	88	35.2%	<LOD	<LOD	<LOD	<LOD	<LOD	0.20	0.44	3.75
14 years	104	78.9%	0.19 (2.43)	<LOD	<LOD	0.12	0.19	0.35	0.54	2.13
18 years	121	54.6%	0.09 (2.63)	<LOD	<LOD	<LOD	0.08	0.17	0.29	2.56
Fasting	48	37.5%	<LOD	<LOD	<LOD	<LOD	<LOD	0.16	0.35	1.00
Non-fasting	73	65.8%	0.10 (2.59)	<LOD	<LOD	<LOD	0.09	0.18	0.27	2.56
Cases only										
26 weeks	26	3.9%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	1.14
5 years	32	46.9%	<LOD	<LOD	<LOD	<LOD	<LOD	0.21	0.39	3.75
14 years	46	76.1%	0.20 (2.45)	<LOD	<LOD	0.13	0.22	0.41	0.54	1.60
18 years	60	58.3%	0.10 (2.96)	<LOD	<LOD	<LOD	0.09	0.19	0.38	2.56
Fasting	23	39.1%	<LOD	<LOD	<LOD	<LOD	<LOD	0.12	0.35	1.00
Non-fasting	37	70.3%	0.11 (3.04)	<LOD	<LOD	<LOD	0.09	0.20	0.42	2.56
Controls only										
26 weeks	45	4.4%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	1.47
5 years	56	28.6%	<LOD	<LOD	<LOD	<LOD	<LOD	0.20	0.44	2.15
14 years	58	81.0%	0.19 (2.43)	<LOD	<LOD	0.11	0.18	0.32	0.56	2.13
18 years	61	50.8%	0.09 (2.32)	<LOD	<LOD	<LOD	0.08	0.17	0.26	0.60
Fasting	25	36.0%	<LOD	<LOD	<LOD	<LOD	<LOD	0.16	0.34	0.60
Non-fasting	36	61.1%	0.09 (2.12)	<LOD	<LOD	<LOD	0.09	0.17	0.20	0.30

AMPA
Wet-weight (µg/L)

Visit	n	% detected	GM (GSD)	Min	10%	25%	50%	75%	90%	Max
Full sample										
26 weeks	71	14.1%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.10	1.50
5 years	91	76.9%	0.15 (2.95)	<LOD	<LOD	0.09	0.10	0.30	0.45	3.90
14 years	105	93.3%	0.45 (2.81)	<LOD	0.10	0.20	0.47	0.93	1.40	3.70
18 years	121	66.9%	0.15 (3.10)	<LOD	<LOD	<LOD	0.10	0.31	0.66	2.90
Fasting	48	54.2%	0.10 (2.41)	<LOD	<LOD	<LOD	0.09	0.20	0.35	0.50
Non-fasting	73	75.3%	0.20 (3.30)	<LOD	<LOD	0.09	0.20	0.41	1.30	2.90
Cases only										
26 weeks	26	19.2%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.10	1.50
5 years	33	81.8%	0.22 (3.42)	<LOD	<LOD	0.09	0.20	0.42	1.30	3.30
14 years	47	93.6%	0.47 (2.89)	<LOD	0.10	0.20	0.54	1.10	1.30	3.70
18 years	60	73.3%	0.17 (3.24)	<LOD	<LOD	<LOD	0.10	0.33	1.25	2.90
Fasting	23	60.9%	0.09 (2.32)	<LOD	<LOD	<LOD	0.09	0.10	0.30	0.48
Non-fasting	37	81.1%	0.25 (3.32)	<LOD	<LOD	0.10	0.20	0.44	1.50	2.90
Controls only										
26 weeks	45	11.1%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.10	0.54
5 years	58	74.1%	0.12 (2.53)	<LOD	<LOD	<LOD	0.10	0.20	0.36	3.90
14 years	58	93.1%	0.44 (2.77)	<LOD	0.10	0.20	0.45	0.93	1.50	2.60
18 years	61	60.7%	0.13 (2.96)	<LOD	<LOD	<LOD	0.10	0.30	0.50	2.00
Fasting	25	48.0%	<LOD	<LOD	<LOD	<LOD	<LOD	0.20	0.35	0.50
Non-fasting	36	69.4%	0.16 (3.20)	<LOD	<LOD	<LOD	0.10	0.38	0.68	2.00

Specific gravity-corrected (µg/L)

Visit	n	% detected	GM (GSD	Min	10%	25%	50%	75%	90%	Max
Full sample										
26 weeks	71	14.1%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.57	1.71
5 years	91	76.9%	0.22 (2.53)	<LOD	<LOD	0.11	0.19	0.38	0.60	3.96
14 years	105	93.3%	0.72 (2.27)	<LOD	0.24	0.48	0.69	1.12	1.84	6.80
18 years	121	66.9%	0.25 (2.46)	<LOD	<LOD	<LOD	0.23	0.42	0.68	2.32
Fasting	48	54.2%	0.21 (1.94)	<LOD	<LOD	<LOD	0.22	0.34	0.48	0.63
Non-fasting	73	75.3%	0.27 (2.76)	<LOD	<LOD	0.13	0.28	0.53	1.28	2.32
Cases only										
26 weeks	26	19.2%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.60	1.71
5 years	33	81.8%	0.31 (3.01)	<LOD	<LOD	0.15	0.30	0.53	1.20	3.96
14 years	47	93.6%	0.78 (2.26)	<LOD	0.32	0.53	0.72	1.07	2.60	6.80
18 years	60	73.3%	0.26 (2.61)	<LOD	<LOD	<LOD	0.24	0.41	1.19	2.32
Fasting	23	60.9%	0.19 (1.93)	<LOD	<LOD	<LOD	0.20	0.34	0.39	0.60
Non-fasting	37	81.1%	0.32 (2.92)	<LOD	<LOD	0.14	0.31	0.62	1.40	2.32
Controls only										
26 weeks	45	11.1%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.57	0.93
5 years	58	74.1%	0.18 (2.13)	<LOD	<LOD	<LOD	0.16	0.28	0.48	2.93
14 years	58	93.1%	0.67 (2.29)	<LOD	0.20	0.40	0.66	1.24	1.84	4.80
18 years	61	60.7%	0.23 (2.31)	<LOD	<LOD	<LOD	0.23	0.44	0.62	1.83
Fasting	25	48.0%	<LOD	<LOD	<LOD	<LOD	<LOD	0.38	0.51	0.63
Non-fasting	36	69.4%	0.23 (2.57)	<LOD	<LOD	<LOD	0.21	0.50	0.68	1.83

Creatinine-adjusted (µg/g creatinine)

Visit	n	% detected	GM (GSD	Min	10%	25%	50%	75%	90%	Max
Full sample										
26 weeks	71	14.1%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.84	2.27
5 years	91	76.9%	0.25 (2.53)	<LOD	<LOD	0.15	0.24	0.37	0.77	4.34
14 years	105	93.3%	0.49 (2.35)	<LOD	0.18	0.28	0.48	0.79	1.38	7.73
18 years	121	66.9%	0.14 (2.30)	<LOD	<LOD	<LOD	0.14	0.22	0.44	1.07
Fasting	48	54.2%	0.12 (1.86)	<LOD	<LOD	<LOD	0.13	0.19	0.23	0.44
Non-fasting	73	75.3%	0.16 (2.56)	<LOD	<LOD	0.08	0.15	0.30	0.63	1.07
Cases only										
26 weeks	26	19.2%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	1.31	2.27
5 years	33	81.8%	0.37 (3.04)	<LOD	<LOD	0.18	0.37	0.58	1.60	4.34
14 years	47	93.6%	0.52 (2.28)	<LOD	0.23	0.32	0.52	0.79	1.34	7.73
18 years	60	73.3%	0.16 (2.26)	<LOD	<LOD	<LOD	0.16	0.25	0.58	1.00
Fasting	23	60.9%	0.12 (1.71)	<LOD	<LOD	<LOD	0.14	0.18	0.20	0.34
Non-fasting	37	81.1%	0.19 (2.49)	<LOD	<LOD	0.10	0.19	0.34	0.72	1.00
Controls only										
26 weeks	45	11.1%	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.84	1.89
5 years	58	74.1%	0.20 (2.09)	<LOD	<LOD	<LOD	0.19	0.31	0.41	2.60
14 years	58	93.1%	0.47 (2.42)	<LOD	0.15	0.24	0.42	1.00	1.71	3.00
18 years	61	60.7%	0.12 (2.31)	<LOD	<LOD	<LOD	0.12	0.20	0.37	1.07
Fasting	25	48.0%	<LOD	<LOD	<LOD	<LOD	<LOD	0.20	0.28	0.44
Non-fasting	36	69.4%	0.13 (2.54)	<LOD	<LOD	<LOD	0.12	0.25	0.46	1.07

[a]Geometric means and standard deviations were not calculated if fewer than 50% of samples were above the detection limit.

Supplemental Table 2. Chi-square tests for differences in detection frequencies of glyphosate and AMPA concentrations measured in urine samples collected from the mother during pregnancy and from the child at 5, 14, and 18 years, CHAMACOS participants in case-control group.

	Glyphosate			AMPA		
Visit	Cases Detected n (%)	Controls Detected n (%)	p-chi	Cases Detected n (%)	Controls Detected n (%)	p-chi
26 weeks[a]	1 (3.9)	2 (4.4)	0.90	5 (19.2)	5 (11.1)	0.34
5 years[a]	15 (46.9)	16 (28.6)	0.08	27 (81.8)	43 (74.1)	0.40
14 years[a]	35 (76.1)	47 (81.0)	0.54	44 (93.6)	54 (93.1)	0.92
18 years	35 (58.3)	31 (50.8)	0.41	44 (73.3)	37 (60.7)	0.14
Fasting	9 (39.1)	9 (36.0)	0.82	14 (60.9)	12 (48.0)	0.37
Non-fasting	26 (70.3)	22 (61.1)	0.41	30 (81.1)	25 (69.4)	0.25

[a]All samples from prenatal, 5-year, and 14-year visits were non-fasting.

Supplemental Table 3. Correlation matrix and p-values of maternal and child urinary concentrations of glyphosate and AMPA, and PUR data from birth to 5 years, CHAMACOS study.

	PUR 0-5 years r (p-value)	**GLY 26 weeks** r (p-value)	**GLY 5 years** r (p-value)	**GLY 14 years** r (p-value)	**GLY 18 years (all)** r (p-value)	**GLY 18 years (non-fasting)** r (p-value)	**AMPA 26 weeks** r (p-value)	**AMPA 5 years** r (p-value)	**AMPA 14 years** r (p-value)	**AMPA 18 years (all)** r (p-value)	**AMPA 18 years (non-fasting)** r (p-value)
PUR 0-5 years	1										
GLY 26 weeks	0.03 (0.80)	1									
GLY 5 years	-0.007 (0.95)	0.005 (0.97)	1								
GLY 14 years	-0.056 (0.61)	0.107 (0.40)	0.120 (0.30)	1							
GLY 18 years (all)	0.021 (0.83)	-0.023 (0.85)	-0.053 (0.62)	0.023 (0.82)	1						
GLY 18 years (non-fasting)	0.071 (0.58)	0.055 (0.73)	0.353 (<0.01)	-0.071 (0.60)	1.00 (<0.01)	1					
AMPA 26 weeks	0.004 (0.97)	0.659 (<0.01)	0.098 (0.40)	0.140 (0.27)	0.042 (0.73)	0.076 (0.63)	1				
AMPA 5 years	0.118 (0.29)	0.140 (0.27)	0.353 (<0.01)	-0.010 (0.93)	0.018 (0.87)	-0.106 (0.45)	0.157 (0.22)	1			
AMPA 14 years	0.149 (0.16)	0.059 (0.64)	-0.096 (0.40)	0.422 (<0.01)	-0.130 (0.20)	-0.046 (0.73)	0.057 (0.66)	-0.020 (0.86)	1		
AMPA 18 years (all)	-0.016 (0.88)	0.175 (0.14)	-0.159 (0.14)	0.129 (0.20)	0.522 (<0.01)	0.552 (<0.01)	0.202 (0.09)	-0.043 (0.69)	0.081 (0.42)	1	
AMPA 18 years (non-fasting)	-0.098 (0.45)	0.118 (0.45)	-0.241 (0.09)	0.035 (0.80)	0.552 (<0.001)	0.552 (<0.01)	0.200 (0.20)	-0.053 (0.71)	0.088 (0.51)	1.00 (<0.01)	1

Supplemental Table 4. Associations of measures of food consumption with urinary glyphosate, AMPA, and glyphosate residue concentrations in maternal and child urine, CHAMACOS study.

	Glyphosate				AMPA				Glyphosate residues[a]		
	Prenatal % detect	5 year % detect	14 year GM ± GSD	18 year GM ± GSD	Prenatal % detect	5 year GM ± GSD	14 year GM ± GSD	18 year GM ± GSD	5 year GM ± GSD	14 year GM ± GSD	18 year GM ± GSD
Food security											
High/marginal	N/A	32.7%	0.32 ± 2.22	0.16 ± 1.89	N/A	0.21 ± 2.57	0.77 ± 2.27	0.26 ± 2.59	0.45 ± 2.30	1.56 ± 2.10	0.59 ± 2.43
Low or very low		38.9%	0.24 ± 2.56	0.18 ± 2.52		0.22 ± 2.51	0.64 ± 2.27	0.23 ± 2.17	0.55 ± 2.34	1.29 ± 2.08	0.57 ± 2.04
p-value		0.55	0.09	0.53		0.86	0.24	0.52	0.28	0.21	0.81
Fast food											
<1 time/week	N/A	36.4%	0.36 ± 2.41	0.18 ± 2.46	N/A	0.21 ± 2.40	0.85 ± 2.22	0.24 ± 2.50	0.44 ± 2.15	1.80 ± 1.98	0.59 ± 2.19
≥1 time/week		35.2%	0.26 ± 2.34	0.16 ± 2.91		0.22 ± 2.64	0.68 ± 2.28	0.25 ± 2.46	0.52 ± 2.44	1.35 ± 2.11	0.58 ± 2.37
p-value		0.91	0.11	0.51		0.76	0.25	0.79	0.39	0.10	0.95
Total calories											
Below median	5.9%	37.8%	0.23 ± 2.53	N/A	14.7%	0.19 ± 2.21	0.71 ± 2.41	N/A	0.44 ± 1.92	1.40 ± 2.23	N/A
Above median	0.0%	32.6%	0.33 ± 2.05		14.7%	0.25 ± 2.82	0.69 ± 2.13		0.53 ± 2.72	1.42 ± 1.93	
p-value	0.15	0.61	0.05		1.00	0.22	0.87		0.29	0.93	
Total carbohydrates											
Below median	5.9%	38.6%	0.23 ± 2.49	N/A	14.7%	0.20 ± 2.42	0.66 ± 2.34	N/A	0.46 ± 2.10	1.32 ± 2.16	N/A
Above median	0.0%	31.8%	0.33 ± 2.08		14.7%	0.23 ± 2.65	0.74 ± 2.20		2.10 ± 0.51	1.51 ± 1.99	
p-value	0.15	0.50	0.04		1.00	0.45	0.53		0.62	0.38	
Whole grains											
Below median	3.0%	33.3%	0.25 ± 2.42	N/A	9.1%	0.21 ± 2.56	0.68 ± 2.19	N/A	0.45 ± 2.26	1.34 ± 2.07	N/A
Above median	2.9%	37.2%	0.30 ± 2.23		20.0%	0.23 ± 2.52	0.72 ± 2.35		0.52 ± 2.39	1.48 ± 2.08	
p-value	0.97	0.70	0.32		0.20	0.61	0.75		0.42	0.53	
Bran											
Below median	N/A	35.6%	N/A	N/A	N/A	0.21 ± 2.57	N/A	N/A	0.45 ± 2.26	N/A	N/A
Above median		34.9%				0.23 ± 2.51			0.52 ± 2.39		
p-value		0.95				0.57			0.40		
Cold cereal											
<1 time/day	2.3%	35.3%	0.28 ± 2.35	N/A	11.6%	0.17 ± 2.15	0.71 ± 2.29	N/A	0.39 ± 1.77	1.42 ± 2.12	N/A
≥1 time/day	7.1%	35.2%	0.25 ± 2.14		17.9%	0.25 ± 2.70	0.60 ± 2.07		0.55 ± 2.60	1.29 ± 1.57	
p-value	0.32	0.99	0.73		0.46	0.06	0.55		0.06	0.70	
Hot cereal											
<1 time/week	3.5%	37.3%	0.25 ± 2.38	N/A	10.3%	0.22 ± 2.45	0.68 ± 2.23	N/A	0.50 ± 2.34	1.32 ± 2.11	N/A
≥1 time/week	4.8%	31.0%	0.40 ± 1.91		16.7%	0.21 ± 2.75	0.78 ± 2.40		0.46 ± 2.30	1.76 ± 1.86	

p-value	0.79	0.56	0.02		0.45	0.79	0.48		0.67	0.10	
Bread											
≤1 time/week	0.0%	36.4%	0.25 ± 2.41	N/A	21.7%	0.21 ± 2.75	0.69 ± 2.22	N/A	0.49 ± 2.41	1.34 ± 2.11	N/A
>1 time/week	6.4%	34.9%	0.36 ± 1.93		10.6%	0.22 ± 2.47	0.74 ± 2.45		0.49 ± 2.30	1.64 ± 1.91	
p-value	0.22	0.90	0.10		0.21	0.91	0.73		1.00	0.26	
Tortillas											
<1 time/day	0.0%	43.6%	N/A	N/A	14.3%	0.21 ± 2.48	N/A	N/A	0.47 ± 2.14	N/A	N/A
≥1 time/day	4.7%	28.6%			14.1%	0.23 ± 2.58			0.49 ± 2.48		
p-value	0.56	0.14			0.99	0.71			0.81		
Legumes											
≤4 times/week	2.6%	36.5%	0.28 ± 2.23	N/A	10.3%	0.21 ± 2.24	0.75 ± 2.16	N/A	0.46 ± 2.03	1.50 ± 1.95	N/A
>4 times/week	6.3%	33.3%	0.27 ± 2.49		18.8%	0.23 ± 2.97	0.62 ± 2.42		0.52 ± 2.75	1.28 ± 2.25	
p-value	0.44	0.76	0.87		0.31	0.77	0.28		0.48	0.29	
Fruit											
Below median	5.9%	N/A	0.24 ± 2.47	N/A	23.5%	N/A	0.67 ± 2.14	N/A	N/A	1.31 ± 2.06	N/A
Above median	0.0%		0.32 ± 2.12		5.9%		0.72 ± 2.40			1.52 ± 2.08	
p-value	0.15		0.07		0.04		0.67			0.33	
Vegetables											
Below median	3.0%	N/A	0.24 ± 2.43	N/A	9.1%	N/A	0.67 ± 2.17	N/A	N/A	1.30 ± 2.06	N/A
Above median	2.9%		0.32 ± 2.18		20.0%		0.72 ± 2.37			1.52 ± 2.08	
p-value	0.97		0.08		0.20		0.67			0.31	

[a]Calculated using the formula: [Glyphosate + (1.5 x AMPA)].

Supplemental Table 5. Agricultural use of glyphosate in Monterey County, California, 2000-2018.

Year	Total glyphosate use (kg)
2000	60,844
2002	56,208
2004	56,483
2006	55,776
2008	53,111
2010	59,983
2012	67,338
2014	77,102
2016	102,142
2018	102,780

Source: CDPR. Pesticide Use Reporting (PUR). Published 2022. https://www.cdpr.ca.gov/docs/pur/purmain.htm.

Supplemental Table 6. Unadjusted[a] RRs and 95% CI for two-fold increases in child urinary glyphosate, AMPA, and glyphosate residue concentrations (specific gravity-corrected, μg/L) and abnormal markers of liver inflammation and metabolic syndrome (and its components) in CHAMACOS young adults in case-control group.

	Glyphosate		AMPA			Glyphosate residues[a]	
Outcome	**14 years (n=103-104)**	**18 years[b] (n=72-73)**	**5 years (n=90-91)**	**14 years (n=104-105)**	**18 years[b] (n=72-73)**	**14 years (n=103-104)**	**18 years[b] (n=72-73)**
Elevated liver transaminases	1.05 (0.88, 1.26)	1.04 (0.91, 1.20)	1.28 (1.08, 1.51)	1.09 (0.92, 1.30)	1.11 (0.96, 1.29)	1.07 (0.88, 1.31)	1.11 (0.95, 1.29)
Metabolic syndrome	1.19 (0.77, 1.82)	1.02 (0.54, 1.94)	1.73 (1.09, 2.75)	1.60 (1.07, 2.40)	1.40 (0.79, 2.47)	1.63 (1.01, 2.65)	1.31 (0.67, 2.55)
High blood pressure	1.27 (0.87, 1.85)	0.92 (0.64, 1.31)	1.09 (0.78, 1.52)	1.47 (0.96, 2.25)	1.03 (0.68, 1.56)	1.51 (0.92, 2.48)	0.99 (0.65, 1.52)
Large waist circumference	0.85 (0.68, 1.06)	1.06 (0.82, 1.37)	1.11 (0.84, 1.45)	1.06 (0.78, 1.44)	1.12 (0.82, 1.52)	0.97 (0.66, 1.42)	1.14 (0.83, 1.56)
High glucose	0.99 (0.70, 1.41)	0.71 (0.30, 1.70)	1.41 (0.71, 2.81)	1.37 (0.87, 2.14)	0.89 (0.41, 1.92)	1.31 (0.76, 2.25)	0.71 (0.23, 2.20)
High triglycerides	1.07 (0.80, 1.44)	1.17 (0.75, 1.82)	1.31 (0.65, 2.64)	1.44 (1.05, 1.97)	1.41 (1.00, 1.99)	1.40 (0.97, 2.02)	1.38 (0.94, 2.03)
Low HDL cholesterol	0.87 (0.71, 1.06)	1.10 (0.88, 1.37)	0.96 (0.76, 1.20)	1.11 (0.88, 1.41)	1.12 (0.90, 1.40)	1.04 (0.78, 1.40)	1.14 (0.90, 1.43)

[a]Calculated using the formula: [Glyphosate + (1.5 x AMPA)].

[b]Limited to participants with non-fasting urine samples.

Supplemental Table 7. Adjusted[a] RRs and 95% CI for two-fold increases in child urinary glyphosate, AMPA, and glyphosate residue concentrations (specific gravity-corrected, μg/L) at 18 years and abnormal markers of liver inflammation and metabolic syndrome (and its components) in CHAMACOS young adults in case-control group (n=120-121).

Outcome	Glyphosate	AMPA	Glyphosate residues[b]
Elevated liver transaminases	1.02 (0.91, 1.15)	1.07 (0.95, 1.22)	1.08 (0.95, 1.23)
Metabolic syndrome	0.94 (0.62, 1.43)	1.22 (0.83, 1.79)	1.16 (0.76, 1.76)
High blood pressure	0.89 (0.65, 1.22)	1.21 (0.87, 1.67)	1.12 (0.81, 1.55)
Large waist circumference	0.91 (0.74, 1.13)	1.02 (0.80, 1.31)	0.98 (0.75, 1.27)
High glucose	1.01 (0.56, 1.83)	1.02 (0.66, 1.57)	1.08 (0.65, 1.79)
High triglycerides	1.14 (0.88, 1.47)	1.48 (1.08, 2.03)	1.39 (1.03, 1.88)
Low HDL cholesterol	0.97 (0.79, 1.18)	1.03 (0.83, 1.27)	0.99 (0.78, 1.26)

[a]Models adjusted for sex, any alcohol consumption at 18 years (yes/no), maternal pre-pregnancy BMI, parental work in agriculture during pregnancy (yes/no), household poverty status at 18 years (above vs below the poverty threshold), food security at 18 years (high/marginal security vs low and very low security).

[b]Calculated using the formula: [Glyphosate + (1.5 x AMPA)].

Supplemental Table 8. Adjusted[a] RRs and 95% CI for two-fold increases in child urinary glyphosate, AMPA, and glyphosate residue concentrations (specific gravity-corrected, μg/L) and abnormal liver enzymes and metabolic syndrome (and its components) in CHAMACOS young adults in the case-control group, excluding those cases with actin smooth muscle antibody or ceruloplasmin outside of normal limits, or who reported binge drinking in the past 30 days.[b]

	Glyphosate		AMPA			Glyphosate residue[c]	
Outcome	**14 years (n=97-98)**	**18 years (n=65-66)**	**5 years (n=87-88)**	**14 years (n=98-99)**	**18 years (n=65-66)**	**14 years (n=97-98)**	**18 years (n=65-66)**
Elevated liver transaminases	1.04 (0.86, 1.25)	1.11 (0.93, 1.34)	1.26 (1.04, 1.53)	1.17 (0.96, 1.43)	1.14 (0.94, 1.38)	1.15 (0.91, 1.44)	1.17 (0.95, 1.44)
Metabolic syndrome	1.23 (0.77, 1.97)	1.03 (0.61, 1.74)	2.15 (1.40, 3.29)	1.78 (1.11, 2.87)	1.30 (0.78, 2.17)	1.86 (1.04, 3.33)	1.24 (0.69, 2.23)
High blood pressure	1.34 (0.81, 2.20)	1.06 (0.75, 1.50)	1.41 (0.82, 2.40)	1.47 (0.92, 2.37)	1.29 (0.81, 2.04)	1.55 (0.88, 2.73)	1.25 (0.83, 1.89)
Large waist circumference	0.88 (0.71, 1.09)	1.12 (0.83, 1.52)	1.11 (0.88, 1.40)	1.15 (0.87, 1.52)	1.21 (0.89, 1.64)	1.06 (0.74, 1.51)	1.27 (0.92, 1.75)
High glucose	0.97 (0.58, 1.64)	1.96 (0.37, 10.46)	4.18 (2.35, 7.41)	1.60 (0.92, 2.79)	8.70 (1.01, 75.22)	1.54 (0.76, 3.09)	3.75 (1.03, 13.70)
High triglycerides	0.96 (0.70, 1.32)	1.25 (0.83, 1.90)	1.39 (0.81, 2.38)	1.51 (1.03, 2.20)	1.70 (1.03, 2.79)	1.40 (0.91, 2.17)	1.70 (1.01, 2.86)
Low HDL cholesterol	0.85 (0.69, 1.04)	1.13 (0.88, 1.43)	0.89 (0.71, 1.12)	1.19 (0.96, 1.49)	1.16 (0.86, 1.56)	1.10 (0.83, 1.45)	1.20 (0.88, 1.63)

[a]Models adjusted for sex, any alcohol consumption at 18 years (yes/no), maternal pre-pregnancy BMI, parental work in agriculture during pregnancy (yes/no), household poverty status at time of visit (above vs below the poverty threshold), food security at time of visit (high/marginal security vs low and very low security).

[b]Low ceruloplasmin: n=1, high actin: n=3, binge drinking in last 30 days: n=5, total exclusions: n=8 (one participant had high actin and had binge drinking).

[c]Calculated using the formula: [Glyphosate + (1.5 x AMPA)].

Supplementary Table 9. Overall p-values for visit X exposure interaction terms in multiple informant models for repeated child urinary glyphosate, AMPA, and glyphosate residue concentrations (specific gravity-corrected, μg/L) at the 5-year, 14-year, and 18-year visits and abnormal markers of liver inflammation and metabolic syndrome (and its components), using mixed-effects Poisson models with a random intercept for each CHAMACOS participant.[a,b]

	Glyphosate (n=121-122)	**AMPA (n=121-122)**	**Glyphosate residues[c] (n=121-122)**
Elevated liver transaminases	0.78	0.67	0.77
Metabolic syndrome	0.91	0.58	0.67
High blood pressure	0.42	0.66	0.56
Large waist circumference	0.13	0.98	0.85
High glucose	0.51	0.46	0.52
High triglycerides	0.11	0.56	0.62
Low HDL cholesterol	0.38	0.20	0.30

[a]Fasting urine samples taken at 18 years are not included in models, but 5-year and 14-year samples are still included for those participants.

[b]Models adjusted for sex, any alcohol consumption at 18 years (yes/no), maternal pre-pregnancy BMI, parental work in agriculture during pregnancy (yes/no), household poverty status at 18 years (above vs below the poverty threshold), food security at 18 years (high/marginal security vs low and very low security).

[c]Calculated using the formula: [Glyphosate + (1.5 x AMPA)].

Supplemental Table 10. Mediation analysis of child body mass (at age 14 years) on the adjusted associations (RR and 95% CI) for two-fold increases in child (ages 14 and 18 years) urinary concentrations (specific gravity-corrected) of **A.** AMPA and **B.** glyphosate residues and abnormal liver enzymes and metabolic syndrome (and its components) in CHAMACOS young adult cases and controls.

A. AMPA

	AMPA at 14 years			AMPA at 18 years (non-fasting samples only)		
	Direct	Indirect	Total	Direct	Indirect	Total
Outcome	RR (95% CI)[a]	RR (95% CI)[a]	RR (95% CI)[a]	RR (95% CI)[a]	RR (95% CI)[a]	RR (95% CI)[a]
Elevated liver transaminases	1.16 (0.98, 1.38)	1.02 (0.97, 1.06)	1.18 (0.98, 1.42)	1.15 (1.02, 1.31)	0.99 (0.92, 1.07)	1.15 (0.99, 1.33)
Metabolic syndrome	1.72 (0.88, 3.37)	1.09 (0.97, 1.23)	1.88 (0.97, 3.64)	1.69 (1.17, 2.45)	1.05 (0.80, 1.37)	1.77 (1.14, 2.75)
High blood pressure	1.51 (0.98, 2.32)	1.08 (0.96, 1.20)	1.62 (1.03, 2.54)	1.14 (0.75, 1.73)	1.03 (0.88, 1.21)	1.17 (0.75, 1.82)
Large waist circumference	1.07 (0.85, 1.37)	1.07 (0.97, 1.18)	1.15 (0.86, 1.54)	1.24 (1.01, 1.51)	1.03 (0.89, 1.19)	1.27 (0.96, 1.68)
High glucose	1.60 (0.90, 2.85)	1.03 (0.97, 1.08)	1.65 (0.92, 2.95)	NA	NA	NA
High triglycerides	1.46 (0.98, 2.18)	1.03 (0.97, 1.10)	1.51 (1.01, 2.24)	1.38 (1.00, 1.92)	1.02 (0.93, 1.11)	1.41 (1.02, 1.94)
Low HDL cholesterol	1.15 (0.93, 1.43)	1.02 (0.98, 1.07)	1.18 (0.95, 1.46)	1.15 (0.89, 1.48)	1.00 (0.99, 1.01)	1.15 (0.89, 1.48)

B. Glyphosate residues

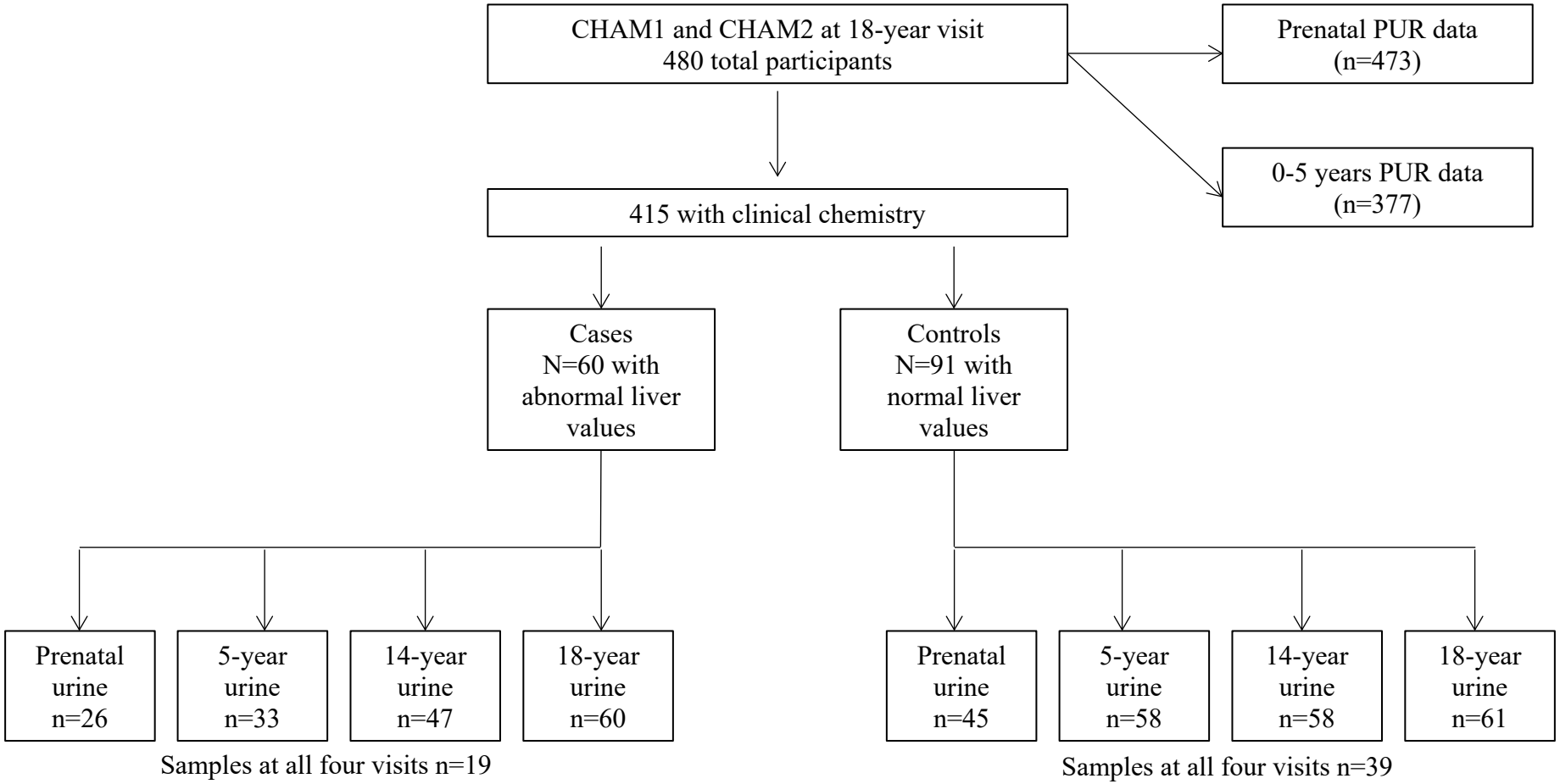
	Glyphosate residues at 14 years			Glyphosate residues at 18 years (non-fasting samples only)[b]		
	Direct	Indirect	Total	Direct	Indirect	Total
Outcome	RR (95% CI)[a]	RR (95% CI)[a]	RR (95% CI)[a]	RR (95% CI)[a]	RR (95% CI)[a]	RR (95% CI)[a]
Elevated liver transaminases	1.16 (0.96, 1.40)	1.00 (0.96, 1.05)	1.16 (0.95, 1.42)	1.18 (1.04, 1.34)	0.99 (0.91, 1.08)	1.17 (1.00, 1.37)
Metabolic syndrome	1.82 (0.87, 3.83)	1.03 (0.91, 1.17)	1.89 (0.90, 3.94)	1.58 (1.07, 2.34)	1.00 (0.75, 1.34)	1.58 (0.98, 2.56)
High blood pressure	1.60 (0.98, 2.63)	1.03 (0.92, 1.15)	1.65 (0.99, 2.74)	1.07 (0.69, 1.66)	1.00 (0.84, 1.20)	1.07 (0.67, 1.71)
Large waist circumference	1.02 (0.77, 1.36)	1.03 (0.93, 1.14)	1.05 (0.75, 1.48)	1.31 (1.07, 1.60)	1.00 (0.85, 1.18)	1.31 (0.98, 1.74)
High glucose	1.53 (0.76, 3.08)	1.01 (0.97, 1.06)	1.55 (0.76, 3.13)	NA	NA	NA
High triglycerides	1.36 (0.87, 2.13)	1.01 (0.96, 1.07)	1.38 (0.89, 2.16)	1.33 (0.96, 1.83)	1.00 (0.91, 1.10)	1.33 (0.97, 1.82)
Low HDL cholesterol	1.08 (0.84, 1.38)	1.01 (0.97, 1.05)	1.09 (0.84, 1.41)	1.20 (0.93, 1.54)	1.00 (1.00, 1.00)	1.20 (0.93, 1.54)

[a]Models adjusted for sex, any alcohol consumption at 18 years (yes/no), maternal pre-pregnancy BMI, parental work in agriculture during pregnancy (yes/no), household poverty status at time of visit (above vs below the poverty threshold), food security at time of visit (high/marginal security vs low and very low security).
[b]Calculated using the formula: [Glyphosate + (1.5 x AMPA)].

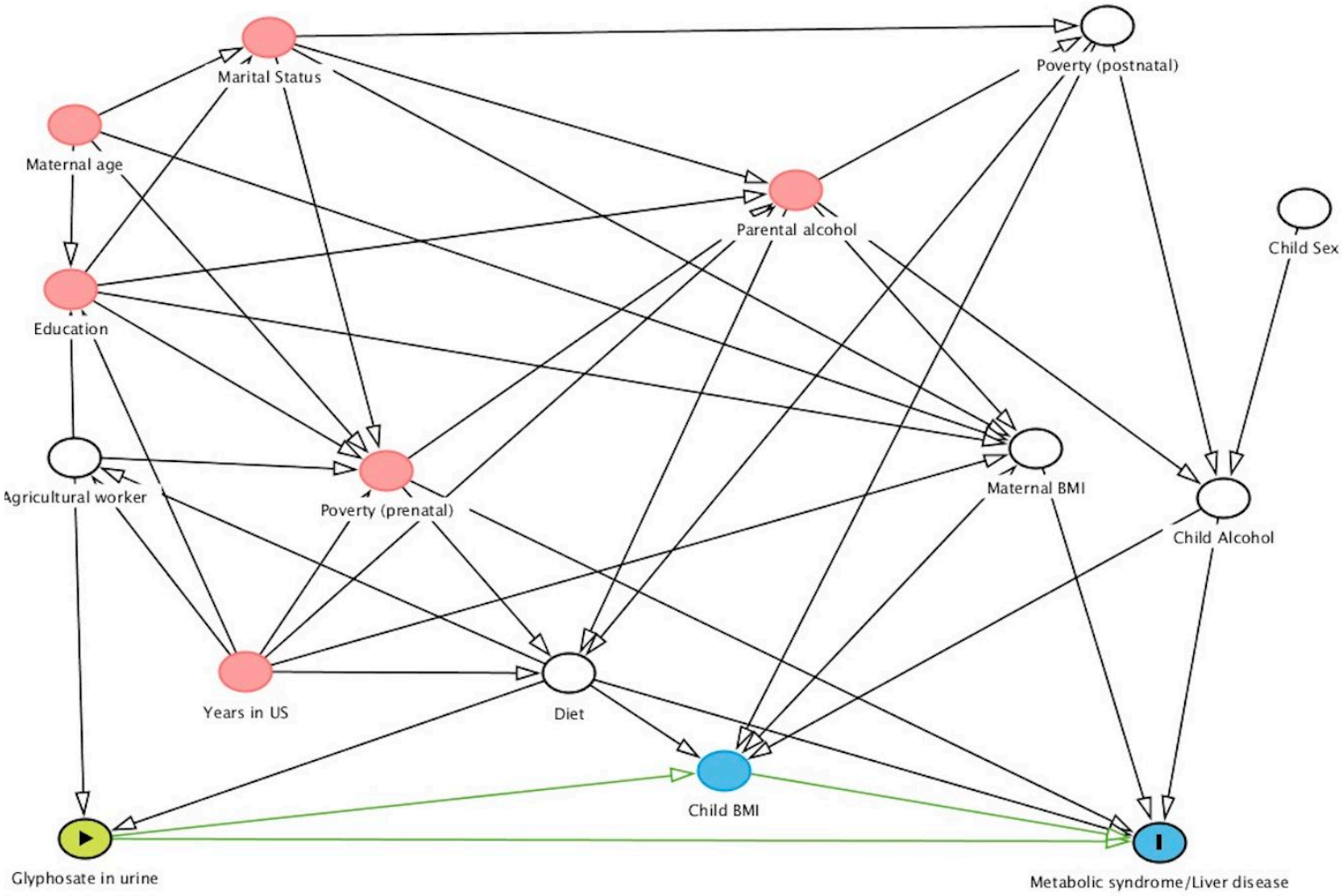
Supplemental Table 11. Unadjusted RRs and 95% CI for living within 1-km of agricultural glyphosate use during maternal pregnancy (any use) and from birth to age 5 years (all use, kg, log_2) based on Pesticide Use Reporting data and abnormal liver enzymes or metabolic syndrome (and its components) among all CHAMACOS young adult participants and in the case-control subset.

	Any PUR use near home residence during pregnancy (yes/no)		**Sum of PUR use near home residence from birth to age 5 years (log_2)**	
Outcome	**All 18-year participants (n=408)**	**Case-control subset (n=150)**	**All 18-year participants (n=329)**	**Case-control subset (n=130)**
Elevated liver transaminases	0.88 (0.55, 1.40)	1.12 (0.75, 1.67)	0.96 (0.82, 1.12)	0.99 (0.87, 1.13)
Metabolic syndrome	1.09 (0.61, 1.93)	3.12 (1.08, 9.01)	1.12 (0.94, 1.33)	1.55 (1.13, 2.14)
High blood pressure	1.04 (0.62, 1.75)	1.11 (0.44, 2.80)	1.00 (0.83, 1.22)	1.18 (0.88, 1.57)
Large waist circumference	1.02 (0.81, 1.28)	1.08 (0.64, 1.83)	1.04 (0.96, 1.12)	0.96 (0.80, 1.14)
High glucose	0.73 (0.30, 1.77)	0.42 (0.12, 1.53)	0.86 (0.66, 1.12)	0.83 (0.60, 1.15)
High triglycerides	1.00 (0.59, 1.70)	3.04 (1.14, 8.10)	1.09 (0.90, 1.32)	1.49 (1.06, 2.09)
Low HDL cholesterol	0.99 (0.77, 1.27)	1.05 (0.63, 1.75)	0.98 (0.90, 1.07)	0.92 (0.77, 1.10)

Supplemental Figure 1. Flow diagram of participants from the CHAMACOS study.



Supplemental Figure 2. Directed Acyclic Graph of the relationship between urinary glyphosate and AMPA concentrations and risk of elevated liver transaminases and metabolic syndrome (and its components).



Supplemental Material. Certificates of INSPQ's participation in the Quebec External Quality Assessment Scheme for Organic Substances in Urine (OSEQAS), German External Quality Assessment Scheme (G-EQUAS), and Human Biomonitoring for Europe (HBM4EU, reference laboratory) program.

German External Quality Assessment Scheme

Intercomparison programme 68, 2021
for toxicological analyses in biological materials

Prof. Dr. med. H. Drexler
on behalf of the German Society for Occupational and Environmental Medicine .e.V

Henkestr. 9-11, D-91054 Erlangen

External Quality Control acc. to the Guidelines of the German Federal Medical Council

Participant: Eric Gaudreau 273
Centre de toxicologie - INSPQ
945, Avenue Wolfe, 4ieme etage
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Canada

Certificate

valid until January 31, 2023

This is to certify you participated in the intercomparison programme 68 / 2021 for occupational / environmental medical - toxicological analyses. In accordance with the guidelines issued by the German Federal Medical Council (Bundesärztekammer) of September 19th, 2014 on implementation of intercomparison programmes in the medical field you have fullfilled the requirements for the following parameters:

Environmental medical field

1-HP in urine	Br2-CA in urine	cis-Cl2-CA in urine
trans-Cl2-CA in urine	Cotinine in urine	Nicotine in urine
p,p'-DDE in serum	DDT in serum	HCB in serum
beta-HCH in serum	gamma-HCH in serum	PCB-28 in serum
PCB-101 in serum	PCB-138 in serum	PCB-153 in serum
PCB-180 in serum	DMP in urine	DMTP in urine
DMDTP in urine	DEP in urine	DETP in urine
DEDTP in urine	5-OH-MEHP in urine	5-oxo-MEHP in urine
5-carboxy-MEPP in urine	MEHP in urine	PFOA in serum
PFOS in serum	1-Naphthol in urine	2-Naphthol in urine
MnBP in urine	MiBP in urine	MBzP in urine
Bisphenol A in urine	3-PBA in urine	FPBA in urine
TCS in urine	Glyphosat in urine	

Erlangen, 2022/01/11

Prof. Dr. med. H. Drexler

Prof. Dr. rer. nat. Th. Göen

German External Quality Assessment Scheme

Intercomparison programme 69, 2022
for toxicological analyses in biological materials

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valid until July 31, 2023

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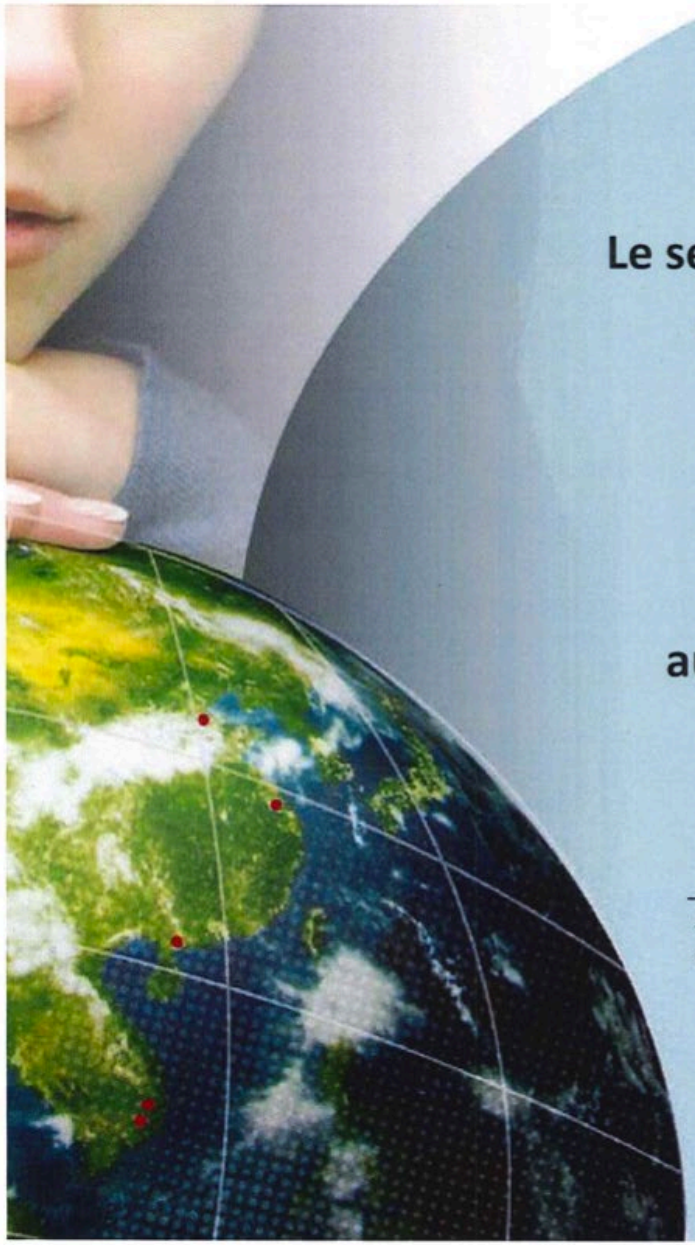
Environmental medical field

PCP in urine	1-HP in urine	Br2-CA in urine
cis-Cl2-CA in urine	trans-Cl2-CA in urine	Cotinine in urine
p,p'-DDE in serum	DDT in serum	HCB in serum
alpha-HCH in serum	beta-HCH in serum	gamma-HCH in serum
PCB-28 in serum	PCB-101 in serum	PCB-138 in serum
PCB-153 in serum	PCB-180 in serum	5-oxo-MEHP in urine
5-carboxy-MEPP in urine	PFOA in serum	PFOS in serum
1-Naphthol in urine	2-Naphthol in urine	MnBP in urine
MiBP in urine	MBzP in urine	Bisphenol A in urine
Trichloropyridinol in urine	Isopropoxyphenol in urine	3-PBA in urine
FPBA in urine	TCS in urine	Glyphosat in urine

Erlangen, 2022/07/12

Prof. Dr. med. H. Drexler

Prof. Dr. rer. nat. Th. Göen



Le secteur des programmes d'assurance qualité externes du CTQ/INSPQ reconnaît la participation de

CTQ 1

au programme OSEQAS pour 2020

Alain LeBlanc
Gestionnaire du programme

David Bisson
Coordonnateur du programme

Institut national de santé publique Québec

Direction de la santé environnementale et de la toxicologie

Programmes d'assurance qualité externes du CTQ/INSPQ

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CTQ 1

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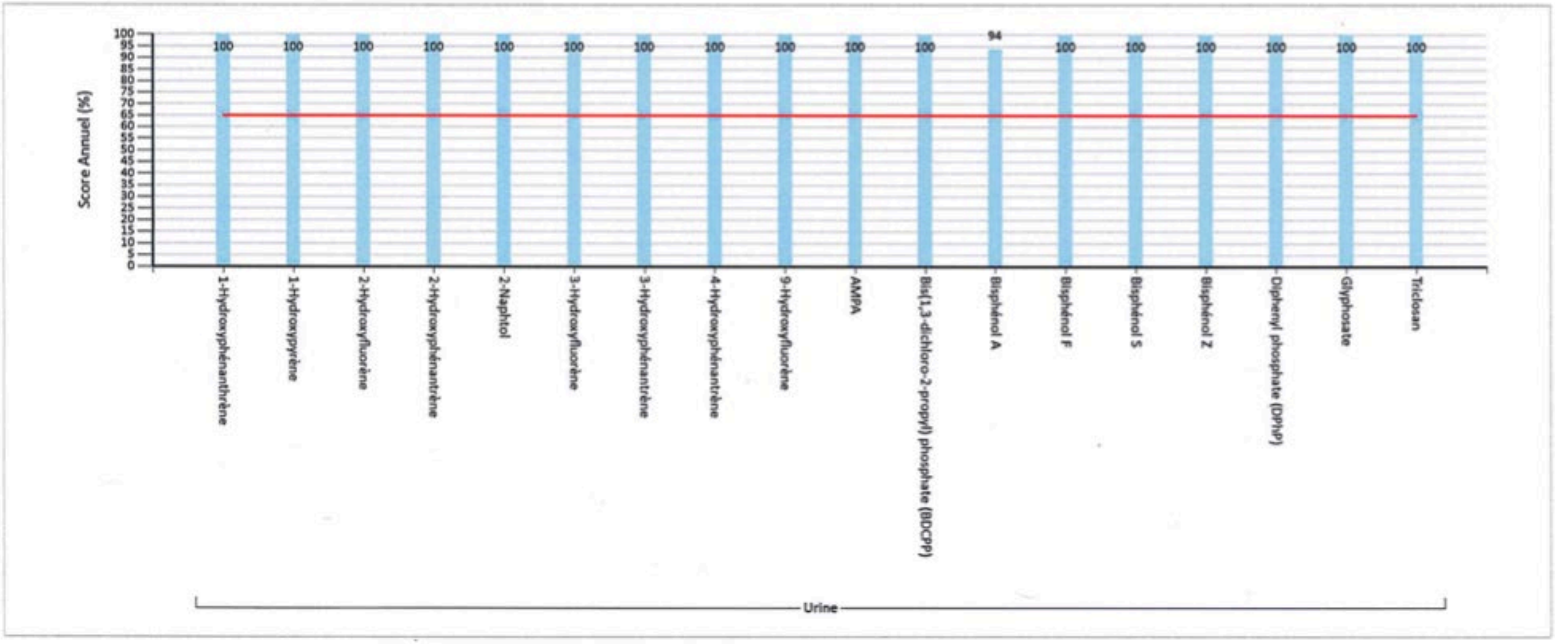
La note accordée (%) correspond au total des points accumulés sur un total maximum de 3 points par résultat. Le score est calculé selon le score Z' en valeur absolue :

3 points si 0.0 < |score Z'| ≤ 1.0 ; 2 points si 1.0 < |score Z'| ≤ 2.0 ; 1 point si 2.0 < |score Z'| < 3.0 ; 0 point si |score Z'| ≥ 3.0

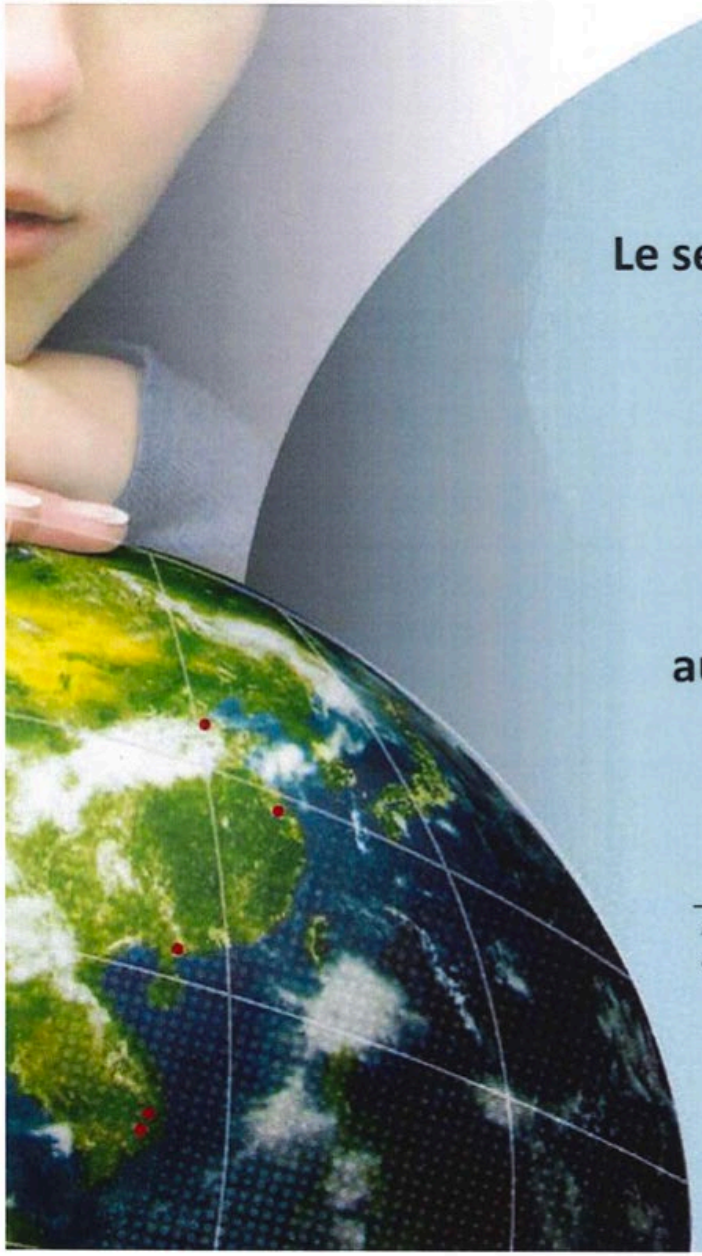
Un score de 0% indique que tous les résultats transmis pour cet analyte/matrice ont reçu un |score Z'| ≥ 3.0. Une absence de score indique qu'aucun résultat numérique n'a été transmis pour cet analyte/matrice.

Le seuil de passage est indiqué au bas du sommaire annuel de performance. Les scores sous le seuil de passage sont inscrits en rouge ou apparaissent sous la ligne du seuil de passage et indiquent une performance insatisfaisante. Nous vous remercions pour votre participation aux programmes d'assurance qualité externes du CTQ/INSPQ et sommes heureux de collaborer avec votre organisation. Pour toute information, n'hésitez pas à communiquer avec nous à ctq@inspq.qc.ca. Il nous fera plaisir de vous assister.



Seuil de passage : 65%

Imprimé le 2021-02-04



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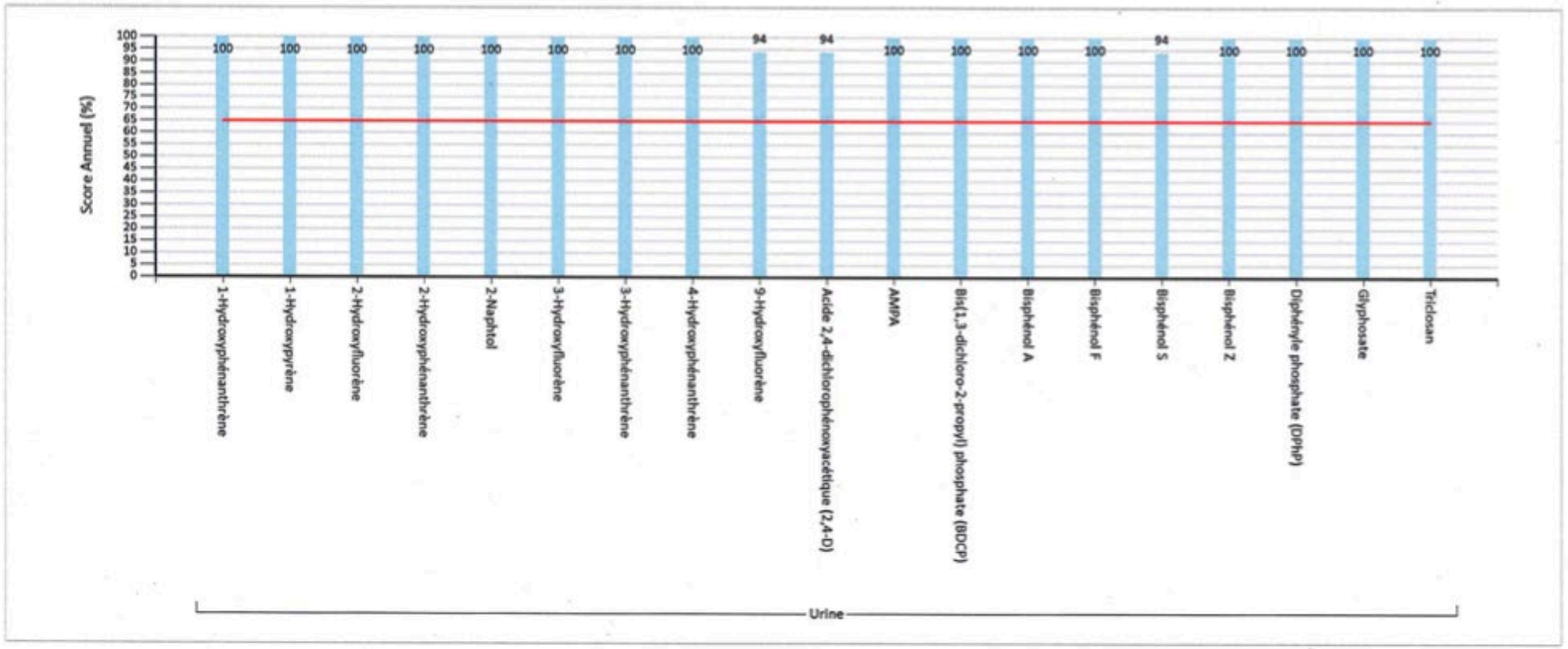

Seuil de passage : 65%

Imprimé le 2021-11-18