

Table S1: Logistic regression models for voluntary interruption of pregnancy by groups

<u>Voluntary interruption pregnancy (N=121)</u>	Unadjusted					Adjusted				
	N	%	OR	IC 95% OR	p-value*	N	%	OR _a	IC 95% OR	p-value*
C±T group	40	33.1	2.80	1.62-4.90	0.00004	39	34.2	3.90	1.48-10.84	0.02
T group	28	23.1	ref			27	23.7	ref		
CTRL group	53	43.8	1.02	0.63-1.69		48	42.1	2.72	1.07-7.20	
C±T group	40	33.1	2.75	1.70-4.42	0.00004	39	34.2	1.44	0.61-3.40	
T group	28	23.1	0.98	0.59-1.59		27	23.7	0.37	0.14-0.93	
CTRL group	53	43.8	ref			48	42.1	ref		
Maternal age at birth										
< 25 years						63	55.3	ref		0.002
≥ 25 years						51	44.7	1.28	0.50-3.41	
Gynaeco-obtetrical history										
yes						84	73.7	0.40	0.23-0.68	0.001
no						30	26.3	ref		
Social coverage										
No health insurance						101	88.6	ref		<0.00001
Health insurance						8	7.0	0.05	0.02-0.10	
CMUc/AME						5	4.4	0.10	0.03-0.24	
Maternal age at birth < 25 years										
C±T group	26	39.7	1.03	0.52-2.04	0.01	25	39.7	3.86	1.46-10.87	0.02
T group	11	15.9	ref			10	15.9	ref		
CTRL group	32	44.4	0.33	0.14-0.73		28	44.4	2.57	1.02-6.84	
C±T group	26	39.7	3.51	1.64-7.33	0.01	23	39.7	1.50	0.64-3.59	0.02
T group	11	15.9	1.75	0.88-3.44		10	15.9	0.39	0.15-0.98	
CTRL group	32	44.4	ref			28	44.4	ref		
Gynaeco-obtetrical history										
yes						12	19.0	0.28	0.12-0.64	0.003
no						51	81.0	ref		
Social coverage										
No health insurance						4	6.3	17.11	5.59-75.22	<0.00001
Health insurance						56	4.8	ref		
CMUc/AME						3	88.9	2.46	0.48-13.99	
Maternal age at birth ≥ 25 years										
C±T group	14	26.9	2.00	0.90-4.37	0.004	14	27.5	1.52	0.60-3.82	0.03
T group	17	32.7	ref			17	33.3	ref		
CTRL group	21	40.4	0.57	0.29-1.13		20	39.2	0.47	0.21-1.04	
C±T group	14	26.9	3.51	1.64-7.33	0.004	14	27.5	3.22	1.30-8.02	0.03
T group	17	32.7	1.75	0.88-3.44		17	33.3	2.12	0.96-4.69	
CTRL group	21	40.4	ref			20	39.2	ref		
Gynaeco-obtetrical history										
yes						18	35.3	0.52	0.24-1.06	0.08
no						33	64.7	ref		
Social coverage										
No health insurance						1	2.0	23.74	9.84-70.95	<0.00001
Health insurance						5	9.8	ref		
CMUc/AME						45	88.2	1.13	0.06-7.34	

Abbreviations: CI: confidence interval; OR: odds ratio; OR_a: adjusted odds ratio; VIP: voluntary interruption of pregnancy; CMUc: Supplementary Health-Care Coverage; AME: state medical assistance; C: cannabis; T: tobacco; CTRL: control; * Wald test

Table S2: Logistic regression models for at least one adverse event during pregnancy by groups

At least one event during pregnancy N=308	Unadjusted					Unadjusted (sub-population with complete BMI data)					Adjusted				
	N	%	OR	IC 95% OR	p-value*	N	%	OR	IC 95% OR	p-value*	N	%	OR _a	IC 95% OR	p-value*
C±T group	70	22.7	0.94	0.59-1.50	<0.00001	43	18.7	1.41	0.74-2.73	0.008	43	18.7	1.70	0.88-3.37	0.002
T group	111	36.0	ref			90	39.1	ref			90	39.1	ref		
CTRL group	127	41.2	0.38	0.26-0.55		97	42.2	0.60	0.38-0.93		97	42.2	0.58	0.36-0.92	
C±T group	70	22.7	2.47	1.62-3.80	<0.00001	43	18.7	2.34	1.28-4.43	0.008	43	18.7	2.93	1.54-5.79	0.002
T group	111	36.0	2.63	1.83-3.81		90	39.1	1.66	1.07-2.59		90	39.1	1.73	1.08-2.78	
CTRL group	127	41.2	ref			97	42.2	ref			97	42.2	ref		
Maternal age at birth (years)											230	100.0	1.05	1.01-1.10	0.01
Pre-pregnancy BMI (kg/m2)											230	100.0	1.05	1.01-1.09	0.01
Nulliparity															
yes											117	50.9	1.80	1.15-2.84	0.01
no											113	49.1	ref		

Single pregnancies; Abbreviations: CI: confidence interval; OR: odds ratio; OR_a: adjusted odds ratio; BMI: body mass index; C: cannabis; T: tobacco; CTRL: control;* Wald test

Table S3: Logistic regression models for composite adverse pregnancy outcome by groups

Composite adverse pregnancy outcome N=186	Univariate					Adjusted				
	N	%	OR	IC 95% OR	p-value*	N	%	OR _a	IC 95% OR _a	p-value*
C±T group	62	33.33	1.12	0.62-2.04	<0.00001	31	18.5	0.86	0.03-22.17	<0.00001
T group	84	45.16	ref			80	47.6	ref		
CTRL group	40	21.51	0.20	0.13-0.31		57	33.9	3.81	0.33-44.10	
C±T group	62	33.33	5.53	3.15-9.87	<0.00001	31	18.5	0.23	0.01-5.22	<0.00001
T group	84	45.16	4.95	3.22-7.68		80	47.6	0.26	0.07-2.88	
CTRL group	40	21.51	ref			57	33.9	ref		
Maternal age at birth (years)						168	100.0	1.07	1.01-1.15	0.29
Nulliparous										
yes						93	55.4	1.72	1.08-2.74	0.02
no						75	44.6	ref		
Social coverage										
No health insurance						19	11.3	1.69	1.04-2.74	0.06
Health insurance						89	53.0	ref		
CMUc/AME						60	35.7	0.90	0.44-1.77	
≤ 28 years (N=89)										
C±T group	18	21.4	1.01	0.48-2.17	0.001	18	22.2	1.01	0.43-2.40	0.002
T group	38	45.2	ref			37	45.7	ref		
CTRL group	28	33.3	0.35	0.19-0.66		26	32.1	0.34	0.18-0.66	
C±T group	18	21.4	2.87	1.36-6.10	0.001	18	22.2	2.94	1.27-6.94	0.002
T group	38	45.2	2.82	1.51-5.34		37	45.7	2.90	1.51-5.70	
CTRL group	28	33.3	ref			26	32.1	ref		
Maternal age at birth (years)						81	100.0	1.03	0.92-1.15	0.61
Nulliparous										
yes						55	67.9	1.39	0.71-2.75	0.34
no						26	32.1	ref		
Social coverage										
No health insurance						37	45.7	1.93	0.97-3.87	0.06
Health insurance						35	43.2	ref		
CMUc/AME						9	11.1	0.74	0.28-1.83	
> 28 years (N=96)										
C±T group	18	18.8	1.67	0.61-5.08	<0.00001	13	14.9	1.14	0.38-3.68	<0.00001
T group	45	46.9	ref			43	49.4	ref		
CTRL group	33	34.4	0.12	0.06-0.22		31	35.6	0.13	0.07-0.25	
C±T group	18	18.8	13.6	5.28-40.07	<0.00001	13	14.9	8.64	3.04-27.11	<0.00001
T group	45	46.9	8.18	4.46-15.39		43	49.4	7.56	4.03-14.56	
CTRL group	33	34.4	ref			31	35.6	ref		
Maternal age at birth (years)						87	100.0	1.00	0.92-1.10	0.91
Nulliparous										
yes						38	43.7	2.20	1.16-4.19	0.02
no						49	56.3	ref		
Social coverage										
No health insurance						10	11.5	1.39	0.67-2.82	0.60
Health insurance						54	62.1	ref		
CMUc/AME						23	26.4	1.42	0.48-4.09	

Single pregnancies; Abbreviations: CI: confidence interval; OR: odds ratio; OR_a: adjusted odds ratio; C: cannabis; T: tobacco; CTRL: control; CMUc: Complementary Universal Health Coverage; AME: state medical assistance; * Wald test

Table S4: Logistic regression models for gestational diabetes by groups

<u>Gestational diabetes</u> <u>N=63</u>	Unadjusted					Unadjusted (sub-population with complete BMI data)					Adjusted				
	N	%	OR	IC 95% OR	p-value*	N	%	OR	IC 95% OR	p-value*	N	%	OR _a	IC 95% OR _a	p-value*
C±T group	11	17.5	1.19	0.52-2.62	0.73	10	18.5	1.79	0.73-4.24	0.41	10	18.5	2.51	0.95-6.51	0.11
T group	19	30.2	ref			16	29.6	ref			16	29.6	ref		
CTRL group	33	52.4	0.89	0.49-1.65		28	51.9	1.15	0.60-2.27		28	51.9	1.02	0.50-2.12	
C±T group	11	17.5	1.33	0.62-2.72	0.73	10	18.5	1.56	0.67-3.40	0.41	10	18.5	1.91	0.82-4.28	
T group	19	30.2	1.12	0.60-2.03		16	29.6	0.87	0.67-3.40		16	29.6	1.16	0.60-2.19	
CTRL group	33	52.4	ref			28	51.9	ref			28	51.9	ref		
Maternal age at birth (years)											54	100.0	1.12	1.05-1.19	
Pre-pregnancy BMI (kg/m2)											54	100.0	1.08	1.04-1.13	
Gynaeco-obtetrical history															
yes											34	63.0	2.03	1.09-3.88	
no											20	37.0	ref		

Single pregnancies; Abbreviations: CI: confidence interval; OR: odds ratio; OR_a: adjusted odds ratio; BMI: body mass index; C: cannabis; T: tobacco; CTRL: control;* Wald test

Table S5: Logistic regression models for at least one neonatal event by groups

<u>At least one neonatal event</u> <u>N=189</u>	Unadjusted					Unadjusted (sub-population with complete pre-pregnancy BMI data)					Adjusted				
	N	%	OR	IC 95% OR	p-value	N	%	OR	IC 95% OR	p-value*	N	%	OR _a	IC 95% OR _a	p-value*
C±T group	41	21.7	1.49	0.80-2.82	<0.00001	31	21.8	2.38	1.07-5.76	<0.00001	31	21.8	2.29	1.02-5.58	<0.00001
T group	76	40.2	ref			65	45.8	ref			65	45.8	ref		
CTRL group	72	38.1	0.27	0.17-0.41		46	32.4	0.24	0.14-0.39		46	32.4	0.24	0.14-14.74	
C±T group	41	21.7	5.56	3.11-10.19	<0.00001	31	21.8	10.11	4.65-24.04	<0.00001	31	21.8	9.39	4.22-22.81	<0.00001
T group	76	40.2	3.73	2.42-5.79		65	45.8	4.24	2.57-7.08		65	45.8	4.10	2.43-7.00	
CTRL group	72	38.1	ref			46	32.4	ref			46	32.4	ref		
Maternal age at birth (years)											142	100.0	0.99	0.94-1.03	0.55
Newborn sex															
girl											73	51.4	ref		0.29
boy											69	48.6	0.77	0.47-1.24	
Pre-pregnancy BMI (kg/m2)											142	100.0	0.99	0.95-1.03	0.60
Gynaeco-obtetrical history															
yes											67	47.2	1.28	0.78-2.11	0.32
no											75	52.8	ref		

Single pregnancies; Abbreviations: CI: confidence interval; OR: odds ratio; OR_a: adjusted odds ratio; BMI: body mass index; C: cannabis; T: tobacco; CTRL: control;* Wald test

Table S6: Logistic regression models for prematurity by groups

Prematurity N=91	Unadjusted					Adjusted				
	N	%	OR	IC 95% OR	p-value*	N	%	OR _a	IC 95% OR _a	p-value*
C±T group	28	30.8	1.71	0.91-3.21	<0.00001	25	27.5	1.65	0.70-3.84	0.85
T group	38	41.8	ref			38	41.8	ref		
CTRL group	25	27.5	0.29	0.17-0.50		28	30.8	0.53	0.24-1.16	
C±T group	28	30.8	5.87	3.10-11.17		25	27.5	3.11	1.32-7.41	
T group	38	41.8	3.43	2.00-5.93		38	41.8	1.89	0.86-4.20	
CTRL group	25	27.5	ref			28	30.8	ref		
Maternal age at birth										
≤ 28 years						45	49.5	ref		0.07
> 28 years						46	50.5	0.51	0.23-1.12	
≤ 28 years (N=45)										
C±T group	14	31.1	1.59	0.67-3.72	0.03	14	31.1	1.59	0.67-3.72	0.05
T group	17	37.8	ref			17	37.8	ref		
CTRL group	14	31.1	0.54	0.24-1.19		14	31.1	0.54	0.24-1.19	
C±T group	14	31.1	3.11	1.32-7.41	0.03	14	31.1	2.93	1.23-7.03	0.05
T group	17	37.8	1.89	0.86-4.20		17	37.8	1.84	0.84-4.10	
CTRL group	14	31.1	ref			14	31.1	ref		
Maternal age at birth (years)						45	100.0	0.94	0.84-1.06	0.32
> 28 years (N=46)										
C±T group	11	23.9	2.14	0.80-5.80	<0.00001	11	23.9	2.10	0.78-5.70	<0.00001
T group	21	45.7	ref			21	45.7	ref		
CTRL group	14	30.4	0.18	0.08-0.38		14	30.4	0.18	0.08-0.38	
C±T group	11	23.9	11.7	4.36-32.65	<0.00001	11	23.9	11.47	4.23-31.87	<0.00001
T group	21	45.7	5.50	2.62-11.90		21	45.7	5.47	2.60-11.84	
CTRL group	14	30.4	ref			14	30.4	ref		
Maternal age at birth (years)						46	100.	0.96	0.86-1.06	0.40

Single pregnancies; Abbreviations: CI: confidence interval; OR: odds ratio; OR_a: adjusted odds ratio; C: cannabis; T: tobacco; CTRL: control; * Wald test

Table S7: Logistic regression models for small for gestational age by groups

Small for gestational age N=89	Unadjusted					Unadjusted (sub-population with complete pre-pregnancy BMI data)					Adjusted				
	N	%	OR	IC 95% OR	p-value*	N	%	OR	IC 95% OR	p-value*	N	%	OR _a	IC 95% OR	p-value*
C±T group	22	24.7	1.03	0.55-1.91	<0.00001	16	23.5	1.28	0.61-2.65	<0.00001	16	23.5	1.14	0.53-2.42	<0.00001
T group	47	52.8	ref			38	55.9	ref			38	55.9	ref		
CTRL group	20	22.5	0.15	0.08-0.27		14	20.6	0.17	0.08-0.32		14	20.6	0.16	0.08-0.32	
C±T group	22	24.7	6.80	3.43-13.62	<0.00001	16	23.5	7.56	3.32-17.55	<0.00001	16	23.5	7.15	3.04-17.16	<0.00001
T group	47	52.8	6.58	3.76-11.89		38	55.9	5.91	3.09-11.87		38	55.9	6.26	3.17-13.03	
CTRL group	20	22.5	ref			14	20.6	ref			14	20.6	ref		
Maternal age at birth (years)											68	100.0	1.03	0.97-1.09	0.31
Pre-pregnancy BMI (kg/m2)											68	100.0	0.96	0.91-1.01	0.13
Newborn sex															
girl											38	55.9	ref		0.21
boy											30	44.1	0.69	0.39-1.23	
Nulliparity															
yes											44	64.7	2.10	1.14-3.93	0.02
no											24	35.3	ref		

Single pregnancies; Abbreviations: CI: confidence interval; OR: odds ratio; OR_a: adjusted odds ratio; BMI: body mass index; C: cannabis; T: tobacco; CTRL: control; * Wald test

Table S8: Logistic regression models for congenital malformations by groups

Congenital malformations, N=47	Unadjusted					Unadjusted (sub-population with complete pre-pregnancy BMI data)					Adjusted				
	N	%	OR	IC 95% OR	p-value*	N	%	OR	IC 95% OR	p-value*	N	%	OR _a	IC 95% OR _a	p-value*
C±T group	10	21.3	1.74	0.71-4.20	0.25	8	20.5	1.94	0.71-5.09	0.28	8	20.5	2.01	0.73-5.32	0.28
T group	13	27.7	ref			12	30.8	ref			12	30.8	ref		
CTRL group	24	51.1	0.89	0.45-1.86		19	48.7	0.96	0.45-2.11		19	48.7	0.98	0.45-2.19	
C±T group	10	21.3	1.95	0.85-4.20	0.25	8	20.5	2.02	0.78-4.85	0.28	8	20.5	2.05	0.77-5.09	0.28
T group	13	27.7	1.12	0.54-2.23		12	30.8	1.04	0.47-2.21		12	30.8	1.02	0.46-2.22	
CTRL group	24	51.1	ref			19	48.7	ref			19	48.7	ref		
Maternal age at birth (years)											39	100.0	1.00	0.94-1.06	0.98
Pre-pregnancy BMI (kg/m2)											39	100.0	1.01	0.96-1.07	0.59

Single pregnancies; Abbreviations: CI: confidence interval; OR: odds ratio; OR_a: adjusted odds ratio; BMI: body mass index; C: cannabis; T: tobacco; CTRL: control * Wald test

Table S9. Description of congenital malformations by groups

Highlighted in grey: medical termination of pregnancy

N° of cases	C±T group (n=10, 21.3%)	T group (n=13, 27.7%)	CTRL group (n=24, 51.1%)
1	- cardiac : atrial septal defect	- cardiac : large ductus arteriosus and atrial septal defect	- cardiac : ventricular septal defect
2	- cardiac : slightly thickened interventricular septum and atrial septal defect	- cardiac : atrial septal aneurysm with persistent foramen ovale	- cardiac : atrial septal defect
3	- cardiac : atrial septal defect - urinary : hypotrophy of the right kidney	- cardiac : asymmetry of the heart chambers, small ductus arteriosus	- cardiac : 2 interventricular septal defects and one atrial septal defect
4	- cardiac : hypoplasia of the left ventricles - peri-thoracic oedema - urinary : méga-bladder	- cardiac : atrial septal defect	- cardiac : dilatation of the right atrium - facial : hygroma coli, facial dysmorphism - genital : hypospadias
5	- urinary : right uropathy	- cardiac : perimembranous interventricular communication	- cardiac : atrial septal defect - osteoarticular : foot slope
6	- osteoarticular : short femoral length (4th percentile)	- cardiac : subrenal agenesis of the inferior vena cava	- urinary : bilateral pyelectasis
7	- osteoarticular : right clubfoot	- urinary : left pyelectasis	- urinary : bilateral pyelectasis
8	- osteoarticular : right clubfoot (according to the geneticist, most likely etiology if folic acid deficiency) - nervous system : microcephaly, bilateral ventriculomegaly, Arnold Chiari 2 abnormality, thoracolumbar spina bifida aperta	- urinary : left renal agenesis, compensatory right renal hypertrophy	- urinary : bilateral pyelectasis
9	- digestive : small bowel atresia	- urinary : polycystic kidneys with ureteral and bladder dilatation, posterior ureteral valves, Potter sequence - pulmonary : hypotrophy of the lung	- urinary : bilateral pyelocaliceal and ureteral dilatation
10	- digestive : enlarged gallbladder - facial : lip occlusion defect, short nasal bones	- digestive : oesophageal atresia	- urinary : uropathy
11		- Walker-Warburg syndrome	- genitals : cryptorchidism
12		- chromosomal : Turner syndrome	- nervous system : proximal spinal muscular atrophy
13		- chromosomal : Di Georges syndrome	- nervous system : hydrocephalus with ventriculomegaly and septal rupture, cerebellar hypoplasia in the sustentorial spaces
14			- nervous system : spina bifida
15			- facial : bilateral cleft lip and palate
16			- digestive : laparochisis
17			- osteoarticular : micromelic and platyspondylic dwarfism (FGFR3 gene mutation)
18			- chromosomal : Noonan syndrome
19			- chromosomal : trisomy 13
20			- chromosomal : trisomy 22
21			- chromosomal : persistent cervical hygroma, suspected ventricular septal defects
22			- other : Left-handedness (Gaucher disease)
23			- other : Beckwith-Wiedemann syndrome
24			- other : congenital nevus

Table S10. Description of adverse events (AEs) in the C±T group

Maternal AEs (N=73)	Fetal AEs (N=13)	Neonatal AEs (N=79)
Threat of preterm delivery (n=11) Gestational diabetes (n=11) Cannabis dependence (n=8) Oligoamnios/anamnios (n=7) Placental abnormalities (n=7): retroplacental hematoma (n=3), placenta previa (n=2), subchorionic hematoma et thrombosis (n=2) Premature rupture of membranes (n=6) Hypertension/Eclampsia/Pre-eclampsia/HELLP syndrome (n=5) Ectopic pregnancy (n=4) Maternal cannabis withdrawal syndrome (n=2) Medical termination of pregnancy (n=2) Miscarriage (n=2) Hemorrhagic stroke (n=1) Reversible posterior encephalopathy syndrome (n=1) Clastic crisis (n=1) Agitation and depressive syndrome (n=1) Sad mood (n=1) Adrenal necrosis (n=1) Abdominal pain (n=1) Folic acid deficiency (n=1)	Fetal heart rhythm disorder (n=12) In utero fetal death (n=1)	Prematurity (n=28) Small for gestational age (n=22) Congenital malformations (n=10) Apgar < 7 at 1 minute (n=6) Respiratory failure (n=4) Stillbirth (n=3) Hypoglycemia (n=3) Bradycardia (n=2) Behaviour problem (n=1)

Single pregnancies. Abbreviations: AE: adverse event