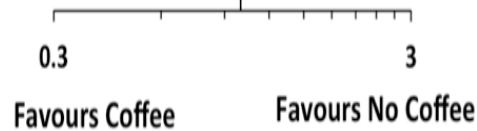


Outcome	Author	Year	No. of events /total	Follow up range (years)	Summary measure	Risk Estimate	Estimate	LCL	UCL	Total studies	Cohort	Case Control	Effects model	Tau ²	I ²	Eggers	AMSTAR
Endometrial Cancer ^{29*}	Zhou	2015	10100/1534039	9-26	RR		0.76	0.69	0.84	13	13	0	R	0.01	28.54	0.03	7
Melanoma ^{30*}	Yew	2016	3327/925484	NP	RR		0.76	0.64	0.91	9	9	0	R	0.03	48.34	0.77	8
Alzheimer's Disease ^{21*}	Liu	2016	NP/NP	5-21	RR		0.73	0.55	0.97	4	4	0	R	0.00	0.00	ND	6
Type II diabetes ^{31b*}	Ding	2014	45335/1109272	1-24	RR		0.70	0.65	0.75	27	27	0	R	0.01	50.28	0.05	7
Oral Cancer ^{7*}	Wang	2016	1910/1395309	6-26	RR		0.69	0.48	0.99	6	6	0	R	0.12	73.67	ND	5
Cirrhosis ^{32*}	Liu	2015	1785/130305	NP	OR		0.69	0.44	1.07	3	3	0	R	0.02	12.91	ND	7
Renal Stones ^{33*}	Wang	2014	NP/126382	NP	RR		0.67	0.56	0.81	2	2	0	R	0.00	0.00	ND	6
Parkinson's Disease ^{34b*}	Qi	2014	2414/894568	NP	RR		0.64	0.53	0.76	7	7	0	R	0.01	15.88	ND	5
Leukaemia ²⁷	Yu	2011	NP ^d	8-11	RR		0.63	0.41	0.84	2	2	0	R	NP	0	NP	5
Post MI Mortality ^{35*}	Brown	2016	604/3271	3.8	RR		0.55	0.45	0.67	2	2	0	R	0.00	8.91	ND	4
Gout ^{36*}	Park	2016	NP/135302	NP	RR		0.50	0.36	0.70	2	2	0	R	0.02	34.90	ND	6
Liver Cancer ^{37*}	Bravi	2016	3414/2267143	10-44	RR		0.50	0.43	0.58	11	11	0	R	0.01	20.00	0.62	6
Chronic Liver Dis. ^{37*}	Bravi	2016	1410/386049	6-19	RR		0.35	0.22	0.56	5	5	0	R	0.20	75.32	ND	6



*Estimates are from our own re-analysis

^a Maximum consumption in a non-linear dose-response analysis

^b p-value for non-linearity significant

^c Not all no. of cases published;

^d Not possible to separate from other outcomes

NP = Not published; ND = Not done N/A = Not appropriate

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Outcome	Author	Year	No. of events /total	Follow up range (years)	Summary measure	Risk Estimate	Estimate	LCL	UCL	Total studies	Cohort	Case Control	Effects model	Tau ²	i ²	Eggers	AMSTAR
CKD ^{54*}	Wijarnp	2016	NP/14898	n/a	RR		0.71	0.47	1.08	4 ^e	0	0	R	0.11	65.98	ND	7
NAFLD ^{55*}	WijarNP	2017	NP/2407	NP	RR		0.71	0.6	0.85	3 ^e	1	1	R	0.00	0.00	ND	7
Liver Cancer ^{37*}	Bravi	2016	3414/2267143	10-44	RR		0.66	0.55	0.78	12	12	0	R	0.06	79.84	0.24	6
Parkinson's Disease ^{56*}	Noyce	2012	1940/719187	10-27	RR		0.64	0.53	0.77	6	6	0	R	0.02	29.00	ND	7
Chronic Liver Dis. ^{37*}	Bravi	2016	1463/437355	6-19	RR		0.62	0.47	0.82	6	6	0	R	0.07	80.25	ND	6
Liver Cirrhosis ^{32*}	Liu	2015	1880/130496	NP	OR		0.61	0.45	0.84	3	3	0	R	0.00	0.00	ND	7

*Estimates are from our own re-analysis

^d Not possible to separate from other outcomes

^e Included cross-sectional studies

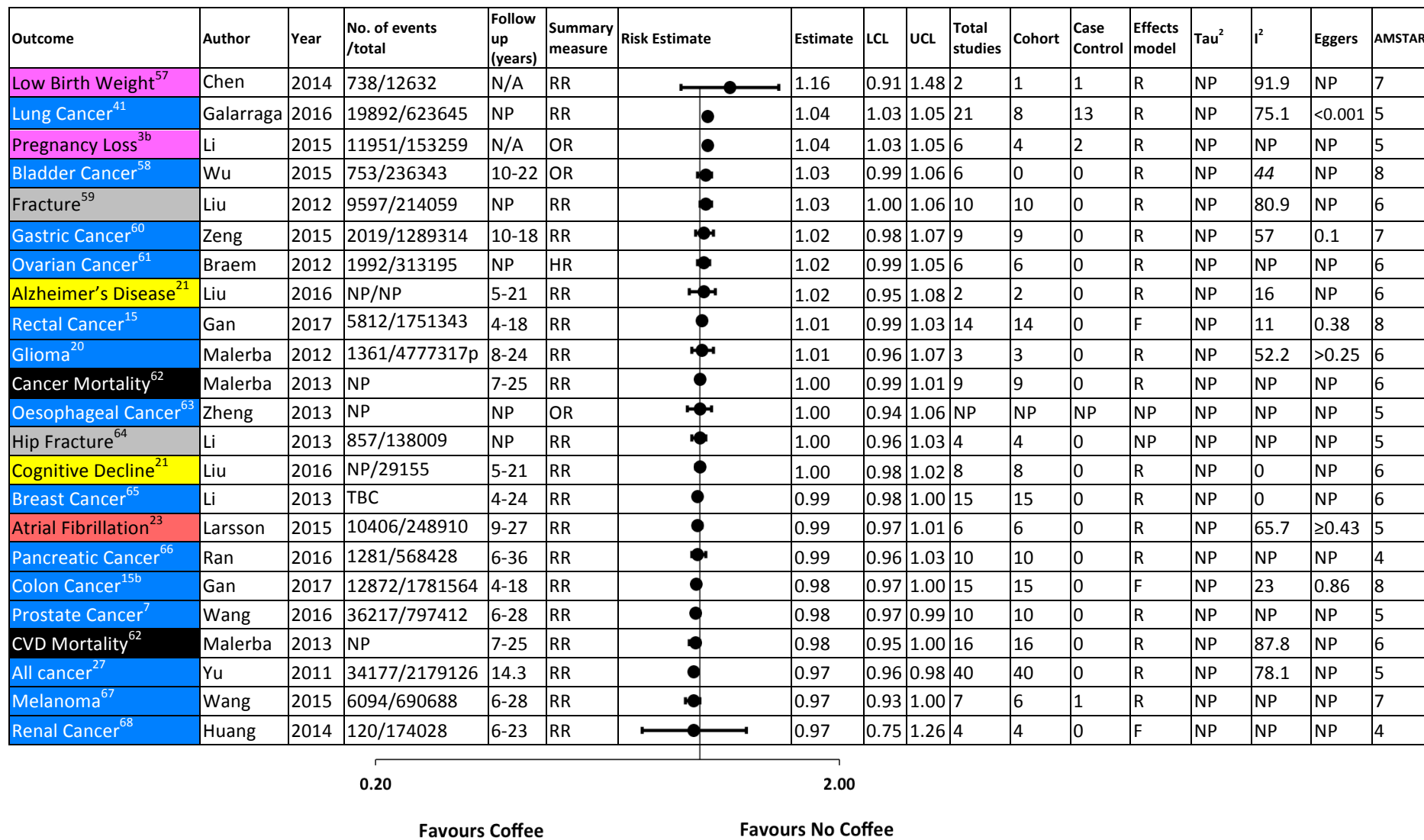
NP = Not published

ND = Not done



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Figure C: Coffee consumption of ONE EXTRA CUP/DAY and associations with multiple health outcomes



Outcome	Author	Year	No. of events /total	Follow up (years)	Summary measure	Risk Estimate	Estimate	LCL	UCL	Total studies	Cohort	Case Control	Effects model	Tau ²	I ²	Eggers	AMSTAR
Colorectal Cancer ^{15b}	Gan	2017	22034/1872460	4-18	RR		0.97	0.92	1.03	17	17	0	R	NP	34.3	0.43	8
All-Cause Mortality ^{69b}	Je	2014	124011/947047	7-25	RR		0.96	0.94	0.97	16	16	0	R	NP	NP	NP	6
Gallstones ^{26b}	Zhang	2015	10911/198831	NP	RR		0.95	0.91	1.00	3	3	0	R	NP	54.5	NP	8
Type II diabetes ⁷⁰	Jiang	2014	46722/974372	2-20	RR		0.94	0.93	0.95	20	20	0	R	NP	NP	NP	8
Endometrial Cancer ⁷	Wang	2016	4730/592672	6-26	RR		0.94	0.92	0.96	11	11	0	NP	NP	NP	NP	5
Depression ⁷¹	Wang	2016	14506/327608	NP	RR		0.92	0.87	0.97	5 ^e	2	1	R	NP	60.4	0.03	6
Renal Stones ³³	Wang	2014	NP/167650	NP	RR		0.91	0.88	0.95	5	3	2	R	NP	42.7	0.18	6
Parkinson's Disease ⁷²	Hernan	2002	459/187281	NP	RR		0.88	0.77	1.00	4	4	0	R	NP	NP	NP	4
Liver Cancer ³⁷	Bravi	2016	3414/2267143	10-44	RR		0.85	0.81	0.90	12	12	0	R	NP	NP	0.17	6
Cirrhosis ⁷³	Kennedy	2016	1364/427687	14-18	RR		0.83	0.78	0.88	5	5	0	R	NP	91.1	NP	9
Cirrhosis Mortality ⁷³	Kennedy	2016	1034/303622	14-18	RR		0.74	0.59	0.86	4	4	0	R	NP	90.3	NP	9
Chronic Liver Dis. ³⁷	Bravi	2016	1463/437355	10-44	RR		0.74	0.65	0.83	6	6	0	R	NP	NP	0.43	6

Nb: No dose response analyses were re-analysed

^b p-value for non-linearity significant

^c Not all no. of cases published;

^d Not possible to separate from other outcomes

^e Included cross-sectional studies

NP = Not published

ND = Not done; N/A = Not appropriate

0.20

2.00

Favours Coffee

Favours No Coffee

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Figure D: Decaffeinated coffee exposure and associations with multiple health outcomes

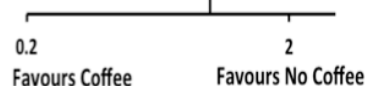
Outcome	Author	Year	No. of events /total	Follow up (years)	Summary measure	Risk Estimate	Estimate	LCL	UCL	Total studies	Cohort	Case Control	Effects model	Tau ²	i ²	Eggers	AMSTAR
ANY versus NONE																	
Urinary Tract Cancer ⁴²	Zeegers	2001	NP	N/A	OR		1.18	0.99	1.4	4	0	4	R	NP	2.4	0.51	5
HIGH versus LOW																	
RheumatoidArthritis ^{4,5*}	Lee	2014	638/113822	11-20	RR		1.71	0.79	3.71	2	2	0	R	NP	71.2	NP	5
Bladder Cancer ⁵⁸	Wu	2015	NP	10-22	OR		1.29	0.88	1.89	5	NP	NP	R	NP	62.7	NP	8
Coronary Heart Dis. ⁷⁴	Sofi	2007	5838/155805	14-20	RR		1.1	0.9	1.34	3	3	0	R	NP	NP	NP	4
NM Skin Cancer ^{28*}	Caini	2017	25413/NP	NP	RR		1.01	0.94	1.1	3	3	0	R	0	0	ND	5
Cardiovascular Dis. ¹⁶	Ding	2014	NP	NP	RR		1.00	0.88	1.14	5	5	0	R	NP	NP	NP	7
Cancer Mortality ^{13a}	Grosso	2016	NP	NP	RR		1.00	0.91	1.09	2	2	0	R	NP	NP	NP	5
Breast Cancer ⁷⁵	Jiang	2013	32790/404188	10-22	RR		0.97	0.89	1.06	12	4	8	F	NP	29.7	NP	5
Parkinson's Disease ³⁴	Qi	2015	1210/251300	NP	RR		0.94	0.78	1.12	4	3	1	NP	NP	NP	NP	6
MalignantMelanoma ⁷⁶	Liu	2016	NP	NP	RR		0.94	0.82	1.08	5	5	0	R	NP	0	0.116	7
All-cause Mortality ^{13a}	Grosso	2016	NP	NP	RR		0.90	0.79	1.01	5	5	0	R	NP	NP	NP	5
CVD Mortality ^{13a}	Grosso	2016	NP	NP	RR		0.86	0.69	1.08	3	3	0	R	NP	NP	NP	5
Type II Diabetes ^{31*b}	Ding	2014	22015/417454	1-24	RR		0.80	0.70	0.91	11	11	0	R	0.03	62	0.13	7
Endometrial Cancer ²⁹	Zhou	2015	3127/363254	9-26	RR		0.77	0.63	0.94	4	4	0	R	NP	0	0.88	7
Lung Cancer ⁷⁷	Tang	2010	NP	NP	RR		0.66	0.54	0.81	2	NP	NP	R	NP	0	NP	5
EXTRA 1 CUP/DAY																	
Endometrial Cancer ²⁹	Zhou	2015	3127/363254	9-26	RR		0.96	0.92	0.99	9	9	0	R	NP	NP	NP	7
Type II Diabetes ³¹	Ding	2014	22015/417454	1-24	RR		0.94	0.91	0.98	14	16	0	R	NP	NP	NP	7
Liver Cancer ⁷⁸	Kenned	2017	800/750000	11-18	RR		0.93	0.86	1.00	3	0	0	R	NP	NP	NP	8

*Estimates from our own reanalysis

^a Maximum consumption in a non-linear dose-response analysis

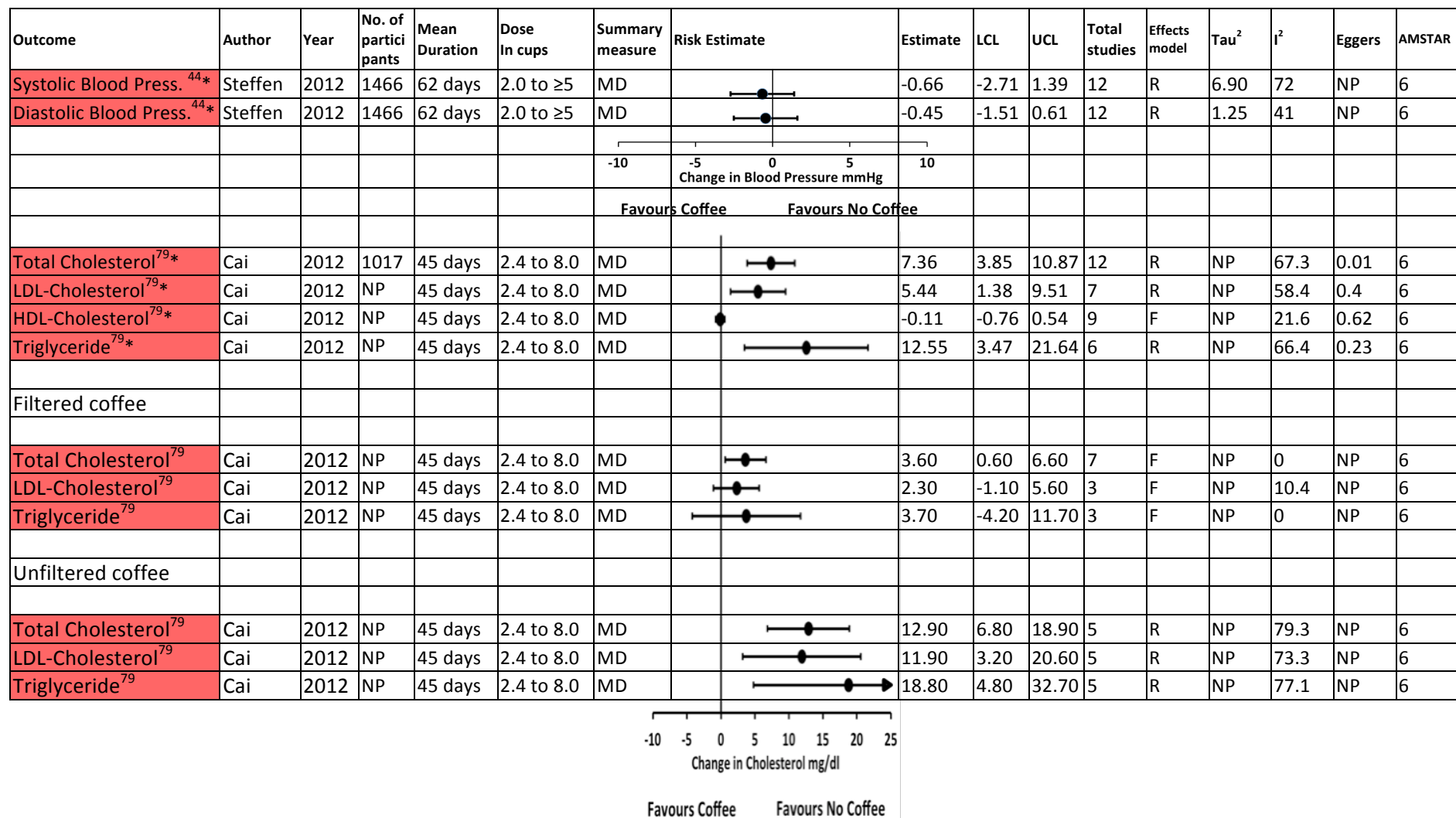
^b p-value for non-linearity significant

NP = Not published; ND = Not done; N/A = Not appropriate



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Figure E: Coffee consumption in randomised controlled trials and multiple health outcomes



Outcome	Author	Year	No. of participants	Mean Duration	Dose In cups	Summary measure	Risk Estimate	Estimate	LCL	UCL	Total studies	Effects model	Tau ²	I ²	Eggers	AMSTAR
Caffeinated coffee																
Total Cholesterol ⁷⁹	Cai	2012	NP	45 days	2.4 to 8.0	MD		9.20	5.00	13.40	12	R	NP	70.7	NP	6
LDL-Cholesterol ⁷⁹	Cai	2012	NP	45 days	2.4 to 8.0	MD		5.50	0.80	10.20	7	R	NP	62.8	NP	6
Triglyceride ⁷⁹	Cai	2012	NP	45 days	2.4 to 8.0	MD		13.80	3.70	24.00	6	R	NP	68.7	NP	6
Decaffeinated coffee																
Total Cholesterol ⁷⁹	Cai	2012	NP	45 days	2.4 to 8.0	MD		3.50	-1.10	8.10	3	F	NP	0	NP	6
LDL-Cholesterol ⁷⁹	Cai	2012	NP	45 days	2.4 to 8.0	MD		6.30	-0.80	13.40	2	F	NP	8.7	NP	6
Triglyceride ⁷⁹	Cai	2012	NP	45 days	2.4 to 8.0	MD		3.50	-10.60	17.70	1	N/A	NP	N/A	N/A	6
							-11 -6 -1 4 9 14 19 24									
							Change in Cholesterol mg/dl									
							Favours Coffee Favours No Coffee									
Preterm Birth ⁸⁰																
Preterm Birth ⁸⁰	Jahanfar	2015	1153	140 days	3.0	RR		0.81	0.48	1.37	1	N/A	N/A	N/A	N/A	9
Small for gest. age ⁸⁰	Jahanfar	2015	1150	140 days	3.0	RR		0.97	0.57	1.64	1	N/A	N/A	N/A	N/A	9
							0.3 Risk Estimate 3									
							Favours Coffee Favours No Coffee									
Birth weight ⁸⁰																
Birth weight ⁸⁰	Jahanfar	2015	1197	140 days	3.0	MD		20.00	-48.70	88.68	1	N/A	N/A	N/A	N/A	9
							-60.00 -10.00 40.00 90.00									
							Mean difference in birth weight (g)									
							Favours Coffee Favours No Coffee									

*Estimates are from our own re-analysis
 NP = Not Published; N/A = Not Appropriate, MD=Mean Difference

Mortality	Cardiovascular	Cancer	Metabolic	Liver & GI	Renal	Pregnancy	Musculoskeletal	Neurological	Gynaecological
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