SYSTEMATIC REVIEW PROTOCOL FOR ANIMAL INTERVENTION STUDIES

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Item #	Section/Subsection/Item	Description	Check for approval
	A. General		
1.	Title of the review	The effects of early-life exposure to endocrine disrupting chemicals on obesity development in rodents: a systematic review.	
2.	Authors (names, affiliations, contributions)	P.N.H. Wassenaar – Design search strategy, in- and exclusion, data extraction, quality and risk of bias assessment, data-analysis, writing paper Prof. dr. ir. J. Legler – Design search strategy, in- and exclusion, data extraction, quality and risk of bias assessment, data-analysis, writing paper	
3.	Other contributors (names, affiliations, contributions)	None	
4.	Contact person + e-mail address	P.N.H. Wassenaar – p.n.h.wassenaar@student.vu.nl	
5.	Funding sources/sponsors	None	
6.	Conflicts of interest	None	
7.	Date and location of protocol registration	07-10-2015 SYRCLE website	
8.	Registration number (if applicable)	Awaiting	
9.	Stage of review at time of registration	Not yet started (but already conducted the database search on 21-9-2015)	
	B. Objectives		
	Background		
10.	What is already known about this disease/model/intervention? Why is it important to do this review?	The prevalence of obesity is increasing worldwide and this development cannot only be explained by an energy imbalance (Heindel & vom Saal, 2009). An accumulating body of evidence, including many rodent exposure studies, suggests that exposure to environmental chemicals/endocrine disrupting chemicals also contribute to this effect. These chemicals are also called obesogens (Grün & Blumberg, 2006). It seems that mainly early-life exposure contributes to the increased prevalence of obesity, since in this period the basis are established for later in life (Legler et al., 2011). Several classes of chemicals are identified as potential obesogenic chemicals, like perfluorinated alkyl acids, plastic associated chemicals, organotins and dioxin-like compounds (Bertuloso et al., 2015; Schmidt, Schaedlich, Fiandanese, Pocar, & Fischer, 2012; Somm et al., 2009; Sugai, Yoshioka, Kakeyama, Ohsako, & Tohyama, 2014; van Esterik et al., 2015). Performing a systematic review on the effects of	

		endocrine disrupting chemicals on obesity in rodents, will provide a systematic overview of the current knowledge on this topic. This review will strengthen the scientific evidence about the effects of environmental chemicals on obesity development, will prevent unnecessary duplication of research and will detect gaps in scientific knowledge. These gaps might result in new directions for new animal experiments. Furthermore, this review might also contribute to the development of new chemical exposure/emission regulations. Such regulations might lead to a better protection of society and reduce obesity related health costs. References: Bertuloso, B. D., Podratz, P. L., Merlo, E., de Araujo, J. F. P., Lima, L. C. F., de Miguel, E. C., … Graceli, J. B. (2015). Tributyltin chloride leads to adiposity and impairs metabolic functions in the rat liver and pancreas. *Toxicology Letters*, *235*(1), 45–59. doi:10.1016/j.toxlet.2015.03.009 Grün, F., & Blumberg, B. (2006). Environmental obesogens: organotins and endocrine disruption via nuclear receptor signaling. *Endocrinology*, *147*, S50–S55. doi:10.1210/en.2005-1129 Heindel, J. J., & vom Saal, F. S. (2009). Role of nutrition and environmental endocrine disrupting chemicals during the perinatal period on the aetiology of obesity. *Molecular and Cellular Endocrinology*. doi:10.1016/j.mce.2009.02.025 Legler, J., Hamers, T., van Eck van der Sluijs-van de Bor, M., Schoeters, G., van der Ven, L., Eggesbo, M., … Trnovec, T. (2011). The OBELIX project: early life exposure to endocrine disruptors and obesity. *American Journal of Clinical Nutrition*. doi:10.3945/ajcn.110.001669 Schmidt, J.-S., Schaedlich, K., Fiandanese, N., Pocar, P., & Fischer, B. (2012). Effects of di(2-ethylhexyl) phthalate (DEHP) on female fertility and adipogenesis in C3H/N mice. *Environmental Health Perspectives*, *120*(8), 1123–9. doi:10.1289/ehp.1104016 Somm, E., Schwitzgebel, V. M., Toulotte, A., Cederroth, C. R., Combescure, C., Nef, S., … Hüppi, P. S. (2009). Perinatal exposure to bisphenol a alters early adipogenesis in the rat. *Environmental Health Perspectives*, *117*, 1549–1555. doi:10.1289/ehp.11342 Sugai, E., Yoshioka, W., Kakeyama, M., Ohsako, S., & Tohyama, C. (2014). In utero and lactational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin modulates dysregulation of the lipid metabolism in mouse offspring fed a high-calorie diet. *Journal of Applied Toxicology : JAT*, *34*(3), 296–306. doi:10.1002/jat.2881 Van Esterik, J. C. J., Sales, L. B., Dolle, M. E. T., Hakansson, H., Herlin, M., Legler, J., & van der Ven, L. T. M. (2015). Programming of metabolic effects in C57BL/6JxFVB mice by in utero and lactational exposure to perfluorooctanoic acid. *Archives of Toxicology*. doi:10.1007/s00204-015-1488-7	

	Research question		
11.	Specify the disease/health problem of interest	Obesity	
12.	Specify the population/species studied	Rodents	
13.	Specify the intervention/exposure	Early-life exposure to endocrine disrupting chemicals. In this systematic review there will be focussed on exposure to five different chemicals: bisphenol A (BPA), tributyltin chloride (TBT), perfluorooctanoic acid (PFOA), mono/bis(2-ethylhexyl) phthalate (MEHP/DEHP) and 2,3,7,8-tetrachloordibenzo-p-dioxin (TCDD).	
14.	Specify the control population	No endocrine disrupting chemical exposure	
15.	Specify the outcome measures	Body weight, triglyceride content, free fatty acid levels, leptin levels, adipose mass and fat (pad) weight.	
16.	State your research question (based on items 11-15)	General research question: Is there a relation between early-life exposure to endocrine disrupting chemicals and obesity development in rodents? More specified research questions: What is the effect of early-life exposure to [chemical A] on [obesity related outcome measure B] in rodents? In which the chemicals are: BPA, TBT, PFOA, MEHP/DEHP or TCDD. And obesity related outcome measures are: body weight, triglyceride content, free fatty acid levels, leptin levels, adipose mass or fat (pad) weight.	
	C. Methods		
	Search and study identification		
17.	Identify literature databases to search (*e.g.* Pubmed, Embase, Web of science)	☒MEDLINE via PubMed ☐Web of Science ☐SCOPUS ☒EMBASE ☐Other, namely: ☐Specific journal(s), namely:	
18.	Define electronic search strategies (*e.g.* use the step by step search guide[15] and animal search filters[20, 21])	For MEDLINE via PubMed and EMBASE: A search strategy has been developed by using the step by step search guide using the search components (SC): SC1, Intervention/exposure: A search strategy for the five investigated chemicals (BPA, TBT, PFOA, MEHP/DEHP and TCDD). SC2, Disease of interest/health problem: Obesity SC3, Animal/animal species/population studied: Rodents For SC3 a modified version of the animal filter of SYRCLE has been used, in which all search terms not related to rodents have been removed.	

		When available, please add a supplementary file containing your search strategy: [Search strategy – PubMed; Search strategy - Embase]	
19.	Identify other sources for study identification	☒Reference lists of included studies ☐Books ☒Reference lists of relevant reviews ☐Conference proceedings, namely: ☐Contacting authors/ organisations, namely: ☐Other, namely:	
20.	Define search strategy for these other sources	Screening the reference lists for relevant titles and screening the abstracts of these relevant titles	
	Study selection		
21.	Define screening phases (*e.g.* pre-screening based on title/abstract, full text screening, both)	Screening phase 1: Screening on title/abstract Screening phase 2: Full text screening	
22.	Specify (a) the number of reviewers per screening phase and (b) how discrepancies will be resolved	Two reviewers for both phases. Discrepancies will be resolved by consulting an independent expert.	
	Define all inclusion and exclusion criteria based on:		
23.	Type of study (design)	Inclusion criteria: • Intervention study (with control group) • Primary study Exclusion criteria: • Non-intervention study (without control group) • Non primary study	
24.	Type of animals/population (*e.g.* age, gender, disease model)	Inclusion criteria: • Healthy rodents Exclusion criteria: • Unhealthy rodents (e.g. ovariectomized rats)	
25.	Type of intervention (*e.g.* dosage, timing, frequency)	Inclusion criteria: • Perinatal (maternal) exposure (during gestation and/or weaning period) • Single chemical exposure Exclusion criteria: • Non perinatal exposure • Mixture exposure • Outcome measured in F2 generation • Outcome measured in fetus (not yet born rodent) • Exposure to the chemical after weaning period (PND21)	
26.	Outcome measures	Inclusion criteria: • Body weight • Triglyceride content • Free fatty acid levels	

		• Leptin levels • Adipose mass • fat (pad) weight Exclusion criteria: • Other outcome measures	
27.	Language restrictions	Inclusion criteria: • English Exclusion criteria: • All other languages	
28.	Publication date restrictions	Inclusion criteria: • All publication dates Exclusion criteria: • None	
29.	Other	Inclusion criteria: • None Exclusion criteria: • Papers of which no free full text is available via VU university or can only be obtained by payment	
30.	Sort and prioritize your exclusion criteria per selection phase	Selection phase 1: Based on title/abstract screening 1. Duplicates 2. Not primary study 3. Not right intervention/exposure (BPA, TBT, PFOA, MEHP/DEHP or TCDD) 4. Not disease of interest/health problem (Obesity) 5. Not a rodent study 6. Not perinatal (maternal) exposure Selection phase 2: Based on full text screening 1. Not primary study 2. Not right intervention/exposure 3. Not disease of interest/health problem (Obesity) 4. Not a rodent study 5. Not perinatal (maternal) exposure 6. Not in English language 7. Outcomes not measured in F1 generation 8. Unhealthy rodents 9. Outcomes measured not of interest	
	Study characteristics to be extracted (for assessment of external validity, reporting quality)		
31.	Study ID (*e.g.* authors, year)	• Authors • Year of publication	
32.	Study design characteristics (*e.g.* experimental groups, number of animals)	• Experimental groups (also type of control intervention) • Number of animals in treatment and control groups • Duration of follow-up, timing of data collection	
33.	Animal model characteristics (*e.g.* species, gender, disease induction)	• Species • Strain • Gender • Type of diet	

34.	Intervention characteristics (*e.g.* intervention, timing, duration)	• Chemical • Life stage of exposure (pre- and/or postnatal) • Dose • Frequency • Duration of exposure • Route of administration/exposure (e.g. diet, drinking water, gavage, sc or ip)	
35.	Outcome measures	• Body weight, triglyceride content, free fatty acid levels, leptin levels, adipose mass and/or fat (pad) weight • Time point at which the outcome measures were measured	
36.	Other (*e.g.* drop-outs)	none	
	Assessment risk of bias (internal validity) or study quality		
37.	Specify (a) the number of reviewers assessing the risk of bias/study quality in each study and (b) how discrepancies will be resolved	Two reviewers will assess the risk of bias. Discrepancies will be resolved by consulting an independent expert.	
38.	Define criteria to assess (a) the internal validity of included studies (*e.g.* selection, performance, detection and attrition bias) and/or (b) other study quality measures (*e.g.* reporting quality, power)	☐By use of SYRCLE's Risk of Bias tool[4] ☒By use of SYRCLE's Risk of Bias tool, adapted as follows: Addition of study quality indicator: Any randomization reported? Y/N Any blinding reported? Y/N ☐By use of CAMARADES' study quality checklist, e.g [22] ☐By use of CAMARADES' study quality checklist, adapted as follows: ☐Other criteria, namely:	
	Collection of outcome data		
39.	For each outcome measure, define the type of data to be extracted (*e.g.* continuous/dichotomous, unit of measurement)	• Body weight – continuous • Triglyceride content – continuous • Free fatty acid levels – continuous • Leptin levels – continuous • Adipose mass – continuous • Fat (pad) weight - continuous	
40.	Methods for data extraction/retrieval (*e.g.* first extraction from graphs using a digital screen ruler, then contacting authors)	1. Extract data from text or tables 2. Extract data from graphs (using digital screen ruler) 3. Contact authors by e-mail for original data in case of missing/unclear data All data will be collected as mean and standard deviation (SD). Standard error of the mean will be recalculated to SD. In case the number of animals is unclear, a conservative estimate will be made. In case the data are reported as median and interquartile range, the authors will be contacted for raw data. In case of missing data and no author contact details, or	

		no response from authors within 3 weeks including a reminder, the study will be omitted from analysis.	
41.	Specify (a) the number of reviewers extracting data and (b) how discrepancies will be resolved	Two reviewers will extract the data. Discrepancies will be resolved by consulting an independent expert.	
	Data analysis/synthesis		
42.	Specify (per outcome measure) how you are planning to combine/compare the data (*e.g.* descriptive summary, meta-analysis)	If possible, a meta-analysis with sub-group analysis will be performed for all outcome measures (body weight, triglyceride content, free fatty acid levels, leptin levels, adipose mass and fat (pad) weight). Otherwise, data will be analysed by descriptive summary.	
43.	Specify (per outcome measure) how it will be decided whether a meta-analysis will be performed	A meta-analysis will be performed if at least 5 studies report on a specific outcome measure for a specific exposure. For subgroup analysis a minimum of 3 studies per subgroup is required.	
	If a meta-analysis seems feasible/sensible, specify (for each outcome measure):		
44.	The effect measure to be used (*e.g.* mean difference, standardized mean difference, risk ratio, odds ratio)	Mean difference & standardized mean difference Where outcomes are measured repeatedly on different points of time in the same animals, we will use the time point at which the measured effect is greatest.	
45.	The statistical model of analysis (*e.g.* random or fixed effects model)	Random effects model	
46.	The statistical methods to assess heterogeneity (*e.g.* I^2, Q)	I^2	
47.	Which study characteristics will be examined as potential source of heterogeneity (subgroup analysis)	The possible causes for heterogeneity will be explored by subgroup analysis • Species • Strain • Gender • Prenatal exposure • Postnatal exposure • Perinatal exposure • Dosage of treatment • Route of exposure • Time of effect • Frequency of exposure	
48.	Any sensitivity analyses you propose to perform	Post hoc subgroup analysis based on excluding the studies with a 'High Risk of selection bias on the domain baseline characteristics'. And/or when a lot of studies examined the effects on more time points: Choose 1 specific time-point for outcome measure, instead of choosing the time-point of greatest efficacy.	
49.	Other details meta-analysis (*e.g.* correction for multiple testing, correction for multiple use of control group)	If for an outcome measure multiple subgroup analyses can be conducted, the p-value for statistical significance will be adjusted to $p<0.01$, to account for potential false positive results.	

50.	The method for assessment of publication bias	Publication bias will be assessed by visually inspecting funnel plots (for outcome measures containing >20 studies).	
Final approval by (names, affiliations):			Date:

Search strategy for PubMed

- The exposure:

“bisphenol A” [tiab] OR BPA [tiab] OR “2,2-bis(4-hydroxyphenyl)propane” [tiab] OR “4,4'-Isopropylidenediphenol” [tiab] OR diphenylolpropane [tiab] OR “4,4'-dihydroxy-2,2-diphenylpropane” [tiab] OR tributyltin [tiab] OR TBT [tiab] OR “tributyltin chloride” [tiab] OR "organotin compounds"[MeSH] OR organotin [tiab] OR "tri-n-butyltin chloride" [tiab] OR tri-n-butyltin [tiab] OR "tributyl tin" [tiab] OR “tri n butyltin” [tiab] OR "perfluorooctanoic acid" [tiab] OR PFOA [tiab] OR "perfluorinated alkyl acids" [tiab] OR "perfluorinated alkyl acid" [tiab] OR "perfluorinated octyl acid" [tiab] OR "perfluorinated octanoic acid" [tiab] OR "pentadecafluorooctanoic acid" [tiab] OR perfluorooctanoate [tiab] OR “diethylhexyl phthalate” [MeSH] OR “diethylhexyl phthalate” [tiab] OR di-2-ethylhexylphthalate [tiab] OR DEHP [tiab] OR "dioctyl phthalate" [tiab] OR "bis(2-ethylhexyl)phthalate" [tiab] OR “mono-(2-ethylhexyl)phthalate” [tiab] OR MEHP [tiab] OR "2 ethylhexyl phthalate" [tiab] OR tetrachlorodibenzodioxin [MeSH] OR tetrachlorodibenzodioxin [tiab] OR TCDD [tiab] OR “2,3,7,8-TCDD” [tiab] OR “2,3,7,8-tetrachlorodibenzo-p-dioxin” [tiab] OR tetrachlorodibenzo-p-dioxin [tiab] OR “endocrine disruptors” [MeSH] OR “endocrine disrupting chemicals” [tiab] OR “endocrine disrupting chemical” [tiab] OR “endocrine disrupting compounds” [tiab] OR “endocrine disrupting compound” [tiab] OR (endocrine [tiab] AND disruptor [tiab]) OR (endocrine [tiab] AND disruptors [tiab]) OR “endocrine disrupter” [tiab] OR “endocrine disrupters” [tiab] OR EDC [tiab] OR EDCs [tiab] OR “environmental chemical” [tiab] OR “environmental chemicals” [tiab] OR “environmental toxicant” [tiab] OR “environmental toxicants” [tiab] OR “environmental toxin” [tiab] OR “environmental toxins” [tiab] OR obesogen [tiab] OR obesogens [tiab] OR “hormone disruptor” [tiab] OR “hormone disruptors” [tiab] OR “endocrine disrupting agent” [tiab] OR “endocrine disrupting agents” [tiab]

- The health problem:

obesity [MeSH] OR obesity [tiab] OR “body fat distribution” [MeSH:noexp] OR adiposity [MeSH] OR adiposity [tiab] OR overweight [MeSH] OR overweight [tiab] OR “Body Mass Index” [MeSH] OR BMI [tiab] OR “quetelet index” [tiab] OR “weight gain” [MeSH] OR “weight gain” [tiab] OR adipogenesis [MeSH] OR adipogenesis [tiab] OR leptin [MeSH] OR leptin [tiab] OR triglycerides [MeSH] OR triglycerides [tiab] OR triglyceride [tiab] OR triacylglycerol [tiab] OR triacylglycerols [tiab] OR “body weight” [MeSH] OR ("body weight" [tiab] NOT "kg body weight" [tiab] NOT "body weight/day" [tiab]) OR obesogenic [tiab] OR “adipose tissue” [MeSH] OR “adipose tissue” [tiab] OR "fat tissue" [tiab] OR “fat pad” [tiab] OR “energy metabolism” [tiab] OR "fatty Acids, Nonesterified" [MeSH] OR “free fatty acids”[tiab] OR FFA [tiab]

- Rodent studies:

“rodentia” [MeSH] OR rodent [tiab] OR rodentia [tiab] OR rodents [tiab] OR mice [tiab] OR mus [tiab] OR mouse [tiab] OR murine [tiab] OR woodmouse [tiab] OR rats[tiab] OR rat [tiab] OR rattus [tiab] OR norvegicus [tiab] OR sigmodon [tiab] OR microtus [tiab] OR murinae [tiab] OR muridae [tiab] OR apodemus [tiab] OR “myodes glareolus” [tiab] OR myodes [tiab] OR cottonrat [tiab] OR cottonrats [tiab] OR hamster [tiab] OR hamsters [tiab] OR mesocricetus [tiab] OR cricetulus [tiab] OR cricetus [tiab] OR cricetinae [tiab] OR “guinea pigs” [tiab] OR “guinea pig” [tiab] OR cavia [tiab] OR “cavia porcellus” [tiab] OR octodon [tiab] OR chinchilla [tiab] OR chinchillas [tiab] OR gerbillinae [tiab] OR gerbil [tiab] OR gerbils [tiab] OR jird [tiab] OR jirds [tiab] OR unguiculatus [tiab] OR jaculus [tiab] OR merione [tiab] OR meriones [tiab] OR sciuridae [tiab] OR squirrel [tiab] OR squirrels [tiab] OR chipmunk [tiab] OR chipmunks [tiab] OR suslik [tiab] OR susliks [tiab] OR sciurus [tiab] OR spermophilus [tiab] OR vole [tiab] OR voles [tiab] OR lemming [tiab] OR lemmings [tiab] OR muskrat [tiab] OR muskrats [tiab] OR lemmus [tiab] OR beaver [tiab] OR beavers [tiab] OR “castor fiber” [tiab] OR “castor canadensis” [tiab] OR jerboa [tiab] OR jerboas [tiab] OR capybara [tiab] OR capybaras [tiab] OR marmot [tiab] OR marmots [tiab] OR cynomys [tiab]

Search strategy for Embase

- The exposure:

“4,4` isopropylidenediphenol”/exp OR “4,4` isopropylidenediphenol”:ab,ti OR “bisphenol A”:ab,ti OR “BPA”:ab,ti OR “2,2-bis(4-hydroxyphenyl)propane”:ab,ti OR “diphenylolpropane”:ab,ti OR “4,4`-dihydroxy-2,2-diphenylpropane”:ab,ti OR "organotin compounds"/exp OR “organotin”:ab,ti OR “tributyltin chloride”:ab,ti OR “tributyltin”:ab,ti OR “TBT”:ab,ti OR "tri-n-butyltin chloride”:ab,ti OR “tri-n-butyltin”:ab,ti OR “tributyl tin”:ab,ti OR “tri n butyltin”:ab,ti OR "perfluorooctanoic acid"/exp OR "perfluorooctanoic acid":ab,ti OR “PFOA”:ab,ti OR "perfluorinated alkyl acids":ab,ti OR "perfluorinated alkyl acid":ab,ti OR "perfluorinated octyl acid":ab,ti OR "perfluorinated octanoic acid":ab,ti OR "pentadecafluorooctanoic acid":ab,ti OR “perfluorooctanoate”:ab,ti OR “phthalic acid bis (2 ethylhexyl) ester”/exp OR “phthalic acid bis (2 ethylhexyl) ester”:ab,ti OR “diethylhexyl phthalate”:ab,ti OR “di 2 ethylhexylphthalate”:ab,ti OR “DEHP”:ab,ti OR "dioctyl phthalate”:ab,ti OR "bis (2 ethylhexyl) phthalate":ab,ti OR “phthalic acid 2 ethylhexyl monoester”/exp OR “phthalic acid 2 ethylhexyl monoester”:ab,ti OR “phthalic acid 2 ethylhexyl ester”:ab,ti OR “mono-(2-ethylhexyl)phthalate”:ab,ti OR “MEHP”:ab,ti OR "2 ethylhexyl phthalate":ab,ti OR “2,3,7,8 tetrachlorodibenzo para dioxin”/exp OR “2,3,7,8 tetrachlorodibenzo para dioxin”:ab,ti OR “tetrachlorodibenzodioxin”:ab,ti OR “TCDD”:ab,ti OR “2,3,7,8-TCDD”:ab,ti OR “2,3,7,8-tetrachlorodibenzo-p-dioxin”:ab,ti OR “tetrachlorodibenzo-p-dioxin”:ab,ti OR “endocrine disruptors”/exp OR “endocrine disrupting chemicals”:ab,ti OR “endocrine disrupting chemical”:ab,ti OR “endocrine disrupting compounds”:ab,ti OR “endocrine disrupting compound”:ab,ti OR (“endocrine”:ab,ti AND “disruptor”:ab,ti) OR (“endocrine”:ab,ti AND “disruptors”:ab,ti) OR “endocrine disrupter”:ab,ti OR “endocrine disrupters”:ab,ti OR “EDC”:ab,ti OR “EDCs”:ab,ti OR “environmental chemical”:ab,ti OR “environmental chemicals”:ab,ti OR “environmental toxicant”:ab,ti OR “environmental toxicants”:ab,ti OR “environmental toxin”:ab,ti OR “environmental toxins”:ab,ti OR “obesogen”:ab,ti OR “obesogens”:ab,ti OR “hormone disruptor”:ab,ti OR “hormone disruptors”:ab,ti OR “endocrine disrupting agent”:ab,ti OR “endocrine disrupting agents”:ab,ti

- The health problem:

“obesity”/exp OR “obesity”:ab,ti OR “body fat distribution”/de OR “adiposity”:ab,ti OR “overweight”:ab,ti OR “body mass”/exp OR “body mass”:ab,ti OR “Body Mass Index”:ab,ti OR “BMI”:ab,ti OR “quetelet index”:ab,ti OR “weight gain”/exp OR “weight gain”:ab,ti OR “weight increase”:ab,ti OR “adipogenesis”/exp OR “adipogenesis”:ab,ti OR “leptin”/exp OR “leptin”:ab,ti OR “obese protein”:ab,ti OR “triacylglycerol”/exp OR “triacylglycerol”:ab,ti OR “triglycerides”:ab,ti OR “triglyceride”:ab,ti OR “triacylglycerols”:ab,ti OR “body weight”/exp OR ("body weight":ab,ti NOT "kg body weight":ab,ti NOT "body weight/day":ab,ti) OR “obesogenic”:ab,ti OR “adipose tissue”/exp OR “adipose tissue”:ab,ti OR "fat tissue":ab,ti OR “fat pad”:ab,ti OR “energy metabolism”:ab,ti OR “free fatty acids”:ab,ti OR “free fatty acid”:ab,ti OR “FFA”:ab,ti

- Rodent studies:

“rodent”/exp OR “rodent”:ab,ti OR “rodents”:ab,ti OR “rodentia”:ab,ti OR “murinae”:ab,ti OR “mouse”:ab,ti OR “mice”:ab,ti OR “mus”:ab,ti OR “murine”:ab,ti OR “woodmouse”:ab,ti OR “muridae”:ab,ti OR “apodemus”:ab,ti OR “rat”:ab,ti OR “rats”:ab,ti OR “rattus”:ab,ti OR “norvegicus”:ab,ti OR “guinea pig”:ab,ti OR “guinea pigs”:ab,ti OR “cavia porcellus”:ab,ti OR “cavia”:ab,ti OR “octodon”:ab,ti OR “hamster”:ab,ti OR “hamsters”:ab,ti OR “cricetinae”:ab,ti OR “mesocricetus”:ab,ti OR “cricetulus”:ab,ti OR “cricetus”:ab,ti OR “gerbil”:ab,ti OR “gerbils”:ab,ti OR “jird”:ab,ti OR “jirds”:ab,ti OR “merione”:ab,ti OR “meriones”:ab,ti OR “unguiculatus”:ab,ti OR “jerboa”:ab,ti OR “jerboas”:ab,ti OR “jaculus”:ab,ti OR “chinchilla”:ab,ti OR “chinchillas”:ab,ti OR “beaver”:ab,ti OR “beavers”:ab,ti OR “castor fiber”:ab,ti OR “castor canadensis”:ab,ti OR “sciuridae”:ab,ti OR “squirrel”:ab,ti OR “squirrels”:ab,ti OR “sciurus”:ab,ti OR “chipmunk”:ab,ti OR “chipmunks”:ab,ti OR “marmot”:ab,ti OR “marmots”:ab,ti OR “suslik”:ab,ti OR “susliks”:ab,ti OR “spermophilus”:ab,ti OR “cynomys”:ab,ti OR “cottonrat”:ab,ti OR “cottonrats”:ab,ti OR “sigmodon”:ab,ti OR “vole”:ab,ti OR “voles”:ab,ti OR “microtus”:ab,ti OR “myodes glareolus”:ab,ti OR “myodes”:ab,ti OR “gerbillinae”:ab,ti OR “lemming”:ab,ti OR “lemmings”:ab,ti OR “lemmus”:ab,ti OR “muskrat”:ab,ti OR “muskrats”:ab,ti OR “capybara”:ab,ti OR “capybaras”:ab,ti