

### Appendix A – PRISMA flow charts for the literature searches

### **PRISMA** flow chart for Q1

Aimed at identifying data on the linoleic acid (LA) and alpha-linolenic acid (ALA) concentrations in from adipose tissue (AT) and their release from AT during weight loss.





### **PRISMA** flow chart for Q2

Aimed at identifying data on the weight loss achieved when consuming total diet replacements for weight control.





#### **PRISMA** flow chart for Q3

Aimed at identifying data on supplemental Mg intake and risk of developing diarrhoea.





### **PRISMA** flow chart for Q4

Aimed at identifying data on intake of dietary fat in energy-restricted diets and risk of gallstone/ biliary sludge formation and gallbladder emptying.





### Appendix B – Studies included in the assessment of the linoleic and alphalinolenic acid concentrations in adipose tissue

The following two forest plots are graphical presentations of the available data on the linoleic acid (LA) and alpha-linolenic acid (ALA) concentrations in adipose tissue. Data are presented for studies published from the year 1990 onwards.

The studies are sorted by ascending point estimates. Each point estimate constitutes the mean fatty acid (FA) concentration for the specific study population, which is also indicated numerically (as percentage) in the seventh column. The 95% confidence interval (CI) around each point estimate is presented by a horizontal line (also indicated in the eight column).

### **B.1.** Linoleic acid concentrations in adipose tissue – studies from 1990

Reference	Country	Gender	Weight status	Sampling site	Ν	mean (95% Cl)	mean	95%-Cl
Scazzocchio et al., 2020	IT	Mixed	Normal-weight	Visceral	17	•	6.82	[6.64; 7.00]
Mamalakis et al., 2004	GR	Males	Mixed + NR	Buttock	78		7.78	[7.54; 8.02]
Mamalakis et al., 2020	GR	Males	Mixed + NR	Buttock	15		8.20	[7.55; 8.85]
Nikolakakis et al., 1999	GR	NR	Mixed + NR	Buttock	27		9.80	[9.19; 10.41]
Mamalakis et al., 2009	GR	Females	Overweight and Obese	Buttock	95		9.83	[9.48; 10.18]
Lundbom et al., 2010	FI	Mixed	Normal-weight	Abdomen	10		9.95	[ 9.62; 10.28]
Tjonneland et al., 1993	DK	Males	Mixed + NR	Buttock	23		10.08	[8.86; 11.30]
Mamalakis et al., 2008 Petrus et al., 2017	GR	Males	Mixed + NR Overweight and Obese	Visceral	146		10.10	9.85; 10.35
Dahm et al., 2011	DK	Females	Mixed + NR	Buttock	544		10.20	[ 9.98; 10.42]
Petrus et al., 2017	SE	Females	Overweight and Obese	Deep SC tissue	75		10.20	[9.89; 10.51]
Mamalakis et al., 2008	GR	Females	Mixed + NR	Buttock	178		10.25	[9.94; 10.56]
Petrus et al., 2017	SE	Females	Overweight and Obese	Superficial SC tissue	75	-	10.33	[10.04; 10.62]
Venø et al., 2013 Kuppenvig et al., 2002a	DK	Mixed	Overweight and Obese	Buttock	25		10.36	[9.93; 10.79]
Lissner et al., 1993	SE	Females	Mixed + NR	Abdomen	20		10.57	[ 9.69; 11.45]
Witt et al., 2010	DK	Females	Mixed + NR	Buttock	22		10.60	[10.15; 11.05]
Dahm et al. 2010		Males	Overweight and Obese Mixed + NR	Buttock	556	-	10.69	[9.63; 11.75]
Witt et al., 2010	DK	Females	Mixed + NR	Buttock	22		10.70	[10.25; 11.15]
Jiang et al, 1999	SE	Males	Mixed + NR	Buttock	123		10.80	[10.47; 11.13]
Pinnick et al., 2012	UK	Males	Mixed + NR	Buttock	18		10.80	[10.21; 11.39]
Due et al., 2008	DK	Mixed	Overweight and Obese	Buttock	30		10.80	[10.41; 11.19]
Tjonneland et al., 1993	DK	Females	Mixed + NR	Buttock	23		10.86	[10.08; 11.64]
Due et al., 2008	DK	Mixed	Overweight and Obese	Buttock	18	İ	10.90	[10.29; 11.51]
Mamalakis et al., 2002b	GR	Males	Mixed + NR	Buttock	123		10.90	[10.57; 11.23]
Kaminskas et al., 1999 Mamalakis et al. 1998	GR	Males	Mixed + NR Mixed + NR	Buttock	50 85		11.00	[10.61; 11.39]
Cottet et al., 2015	FR	Mixed	Mixed + NR	Abdomen	223	- E	11.08	[10.73; 11.43]
Pinnick et al., 2012	UK	Females	Mixed + NR	Abdomen	18		11.10	[10.12; 12.08]
Biong et al., 2010	NO	Mixed	Mixed + NR	Buttock	98		11.10	[10.80; 11.66]
Pedersen et al., 2000	NO	Mixed	Mixed + NR	Buttock	98	-	11.23	[10.80; 11.66]
Kotronen et al., 2010 Kaminskas et al. 1999	臣	Mixed	Overweight and Obese Mixed + NP	Visceral	8		11.24	[10.08; 12.40]
Pinnick et al., 2012	UK	Females	Mixed + NR	Buttock	18		11.50	[10.52; 12.48]
Zatonska et al., 2012	PL	Males	Mixed + NR	Buttock	23		11.62	[10.50; 12.74]
Mamalakis et al. 2014	GR	Females	Mixed + NR	Buttock	80		11.80	[11.21; 12.39]
Mamalakis et al., 1998	GR	Females	Mixed + NR	Buttock	59		12.00	[11.47; 12.53]
Mamalakis et al., 2006	GR	Males	Mixed + NR	Buttock	59		12.00	[11.41; 12.59]
Roberts et al., 1993	UK	Males	Mixed + NR	Abdomen	292		12.05	[11.65; 12.55]
Zatonska et al., 2012	PL	Females	Mixed + NR	Buttock	23		12.10	[11.57; 12.63]
Mamalakis et al., 2006 Kunesova et al. 2012	GR 7 EU countries + UK	Females Mixed	Mixed + NR Overweight and Obese	Abdomen	195		12.40	[10.83; 13.97]
Zatonska et al., 2012	PL	Males	Mixed + NR	Buttock	22	· · · · · · · · · · · · · · · · · · ·	12.57	[11.79; 13.35]
Iggman et al., 2016	SE	Males	Mixed + NR	Buttock	853		12.70	[12.50; 12.90]
Kunesova et al., 2015	CZ	Females	Overweight and Obese	Abdomen	8		13.00	[12.45; 13.55]
Zatonska et al., 2012	PL	Females	Mixed + NR	Buttock	27		13.10	[12.00; 14.20]
Hodson et al., 2014 Kunesova et al. 2015	CZ	Females	Mixed + NR Overweight and Obese	Abdomen	23		13.10	[12.12; 14.08]
Cruz et al., 2001	UK	Mixed	Mixed + NR	Abdomen	8		13.38	[11.73; 15.03]
Ohrvall et al., 1994 Walker et al., 2015	SE	Mixed	Mixed + NR Mixed + NR	Buttock	110		13.40	[13.09; 13.71]
Cruz et al., 2001	UK	Mixed	Mixed + NR	Abdomen	9		13.55	[11.96: 15.14]
Cantwell et al., 2005	IE	Mixed	Mixed + NR	Abdomen	84	i	13.80	[13.27; 14.33]
Pennekes et al., 1993 PenneSpiiders and Blook 1995	NL	Females	Mixed + NR Overweight and Obese	Abdomen	34		14.20	[13.55; 14.85]
Boue et al., 2000	FR	Females	Mixed + NR	Abdomen	71	:	14.35	[13.64; 15.06]
Garaulet et al., 2011	ES	Mixed	Overweight and Obese	Abdomen	20		14.60	[12.62; 16.58]
Garaulet et al., 2001	ES	Mixed	Overweight and Obese	Perivisceral	57		14.82	[13.59; 16.05]
Garaulet et al., 2011	ES	Mixed	Overweight and Obese	Visceral	20		15.00	[13.51; 16.49]
Gruz et al., 2001 Garaulet et al. 2001	ES	Mixed	Mixed + NK Overweight and Obese	Abdomen	76		15.03	[13.31; 16.75]
Halliwell et al., 1996	ŪK	Females	Normal-weight	Abdomen	8		15.12	[13.22; 17.02]
Garaulet et al., 2011	ES	Mixed	Overweight and Obese	Abdomen	20		15.30	[13.50; 17.10]
Garaulet et al., 2001	ES	Mixed	Overweight and Obese	Visceral	24		15.70	[14.28; 17.46]
Sledzinski et al., 2013	PL	Females	Overweight and Obese	Abdomen	16		16.00	[14.67; 17.33]
Hernandez-Morante et al., 2011	ES ES	Mixed	Overweight and Obese	Abdomen	20		16.23 16.37	[15.19; 17.27]
Garaulet et al., 2011	ËŠ	Mixed	Overweight and Obese	Visceral	20		16.40	[14.83; 17.97]
Garaulet et al., 2011	ES	Mixed	Overweight and Obese	Visceral	20		17.10	[15.22; 18.98]
Sledzinski et al., 2013	PL	Females	Overweight and Obese	Visceral	16		18.00	[16.63; 19.97]
Lopes et al., 2007	PT	Mixed	Mixed + NR	Buttock	49		19.10	[17.98; 20.22]
Petrova et al., 2011 Petrova et al., 2011	BG	Females	Mixed + NK Mixed + NR	Buttock	50 58	· · · ·	25.20	[24.18; 26.22]
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### B.2. Alpha-linolenic acid concentrations in adipose tissue – studies from 1990

Footnotes to Appendices B.1 and B.2. BG = Bulgaria; CH = Switzerland; CI = confidence interval; CZ = Czechia; DE = Germany; DK = Denmark; ES = Spain; EU = European Union; FI = Finland; FR = France; GR = Greece; IE = Ireland; IT = Italy; LT = Lithuania; Mixed = study populations consisting of mixtures of weight statuses; N = number of subjects in the study population; NL = Netherlands; NO = Norway; NR = not reported; PL = Poland; PT = Portugal; RU = Russia Federation; SC = subcutaneous; SE = Sweden; UK = United Kingdom.



### Appendix C – Scatter plots of fatty acid concentrations in adipose tissue

The following scatter plots depict how the linoleic acid (LA) and alpha-linolenic acid (ALA) concentrations in adipose tissue are affected by a number of variables, i.e. gender, country, year of study conduct, weight status, health status, sampling site, unit of measurement and some combinations of these criteria.



### C.1. Mean linoleic acid concentration in adipose tissue by gender

# C.2. Mean linoleic acid concentration in adipose tissue by gender and country





# C.3. Mean linoleic acid concentration in adipose tissue by gender and year of study conduct



# C.4. Mean linoleic acid concentration in adipose tissue by weight status



# C.5. Mean linoleic acid concentration in adipose tissue by weight status collapsed into three categories (called in the following simplified)



C.6. Mean linoleic acid concentration in adipose tissue by weight status (simplified) and year of study conduct







### C.7. Mean linoleic acid concentration in adipose tissue by health status

# C.8. Mean linoleic acid concentration in adipose tissue by sampling site





# C.9. Mean linoleic acid concentration in adipose tissue by unit of measurement



# C.10. Mean alpha-linolenic acid concentration in adipose tissue by gender





# C.11. Mean alpha-linolenic acid concentration in adipose tissue by gender and country



C.12. Mean alpha-linolenic acid concentration in adipose tissue by gender and year of study conduct





# C.13. Mean alpha-linolenic acid concentration in adipose tissue by weight status

C.14. Mean alpha-linolenic acid concentration in adipose tissue by weight status (simplified)





# C.15. Mean alpha-linolenic acid concentration in adipose tissue by weight status (simplified) and year of study conduct



C.16. Mean alpha-linolenic acid concentration in adipose tissue by health status



# C.17. Mean alpha-linolenic acid concentration in adipose tissue by sampling site



## C.18. Mean alpha-linolenic acid concentration in adipose tissue by unit of measurement



Abbreviations to Appendices C. BE = Belgium; BG = Bulgaria; CH = Switzerland; CZ = Czechia; DE = Germany; DK = Denmark; ES = Spain; FA = fatty acids; FI = Finland; FR = France; GDR = German Democratic Republic; GR = Greece; IE = Ireland; IT = Italy; LT = Lithuania; Mixed (Gender) = males and females; NL = Netherlands; NO = Norway; NR = not reported; PL = Poland; PT = Portugal; RU = Russia Federation; SC = subcutaneous; SE = Sweden; TG = triglycerides; UK = United Kingdom.



### Appendix D – Protocol for the assessment of additional scientific evidence in relation to the composition of total diet replacements for weight control with respect to linoleic acid and alpha-linolenic acid as well as magnesium

#### Assessment questions and subquestions

The following protocol has been developed in line with current EFSA methodology (EFSA, 2020). As described in the 2020 EFSA 'Draft framework for protocol development for EFSA's scientific assessments', the extent of planning ahead of the assessment is determined as 'low' in order to accommodate the deadline (February 2021) and resources available, although this does not affect the complexity of the subject and of the methodologies to be applied.

In order to answer the Terms of Reference (ToR) as interpreted in Section 1.2 of the statement, the Panel considers that the following questions and subquestions need to be answered.

#### For point A (Section 1.2):

A.1. What is the amount of linoleic acid (LA) and alpha-linolenic acid (ALA) stored in adipose tissue (AT) in overweight and obese individuals living in Europe?

In order to identify the scientific evidence relevant for the assessment, the following subquestions may need to be answered:

- Do the methods for fat store measurement influence the results and, if so, what are the effects?
- Is the LA and ALA concentration in AT proportionally different between normal weight, overweight and obese individuals?
- Are the LA and ALA concentrations/proportions in AT different between different body sites (i.e. does the sampling site influence the assessment of the data), if so, what would be appropriate sampling sites in overweight and obese (not normal weight)?
- What are the fat stores that are released first during weight loss?
- What is the amount of LA and ALA that is released from AT during weight loss?
- How is the proportion of LA and ALA in AT affected by:
  - lifestyle factors (i.e. diet, physical activity)
  - gender,
  - age,
  - ethnicity,
  - and/or diseases (i.e. hypertension, type 2 diabetes mellitus (T2DM), hyperlipidaemia, cardiovascular diseases) in the overweight and obese? If so, which disease(s)? In this context, it should also be considered that overweight and obese individuals consuming total diet replacements for weight control (TDRs) under medical supervision may not only be healthy individuals.
- Does medication intake for the diseases listed above influence the LA and ALA concentration of AT?
- To what extent are LA and ALA released from AT during weight loss reutilised?

A.2. Is there preferential release of certain fatty acids (FA) from AT during weight loss?

In addition to all potential influencing factors listed above that could also influence the release of LA and ALA from AT, the following sub-questions may need to be answered to identify the relevant scientific evidence:

- Does the release of LA and ALA from AT depend on the duration of energy restriction and/or intensity of weight loss?
- Is there preferential release from certain fat depots?
- What are appropriate study designs? Do subjects necessarily need to have lost weight or is a fasting state sufficient? What are the appropriate techniques to measure FA release from AT?
- What is the expected range of weight loss in overweight and obese individuals consuming TDRs?



#### For point C (Section 1.2):

C.1. What is the lowest fat content consumed in an energy-restricted diet that does not give rise to concern with respect to an increased risk of gallstone formation?

#### For points D (Section 1.2):

D.1. What is the amount of supplemental magnesium (Mg) consumed in the context of a diet (i.e. not on an empty stomach) that does not give rise to concern with respect to an increased risk of diarrhoea?

D.2. Is this amount different from the amount of supplemental Mg consumed on an empty stomach that does not give rise to concern with respect to an increased risk of diarrhoea?

#### For points B and E (Section 1.2):

These questions will be answered based on the outcome of the comprehensive literature searches for point A) and D), respectively.

#### Method for the study selection for inclusion/exclusion

The questions listed above will be answered based on a comprehensive literature search. The literature screening will be done in parallel and duplicates (first come first served basis) using DistillerSR<sup>®</sup> (Evidence Partners, Ottawa, Canada). Conflicts that may arise will be discussed and resolved internally during the screening process. Following the screening, the references will be exported to EndNote<sup>®</sup>. Reasons for exclusion at full-text level will be recorded.

The comprehensive literature searches will be conducted by EFSA's information specialist in Embase and PubMed. No limitations on publication date (except for the search on gallstone formation) will be applied but limited to publications in English due to translation constraints.

Search strings are provided in Appendix E with numbers of items identified prior to deduplication. Hand search will be undertaken through the comprehensive reviews and meta-analyses excluded during the screening but identified (with a label in Distiller) as potentially useful for this assessment. In addition, data that could be provided spontaneously by stakeholders and interested parties will be screened for their eligibility. Regarding Mg, previously published scientific reports of officially recognised scientific bodies, and the studies therein, e.g. SCF (2001) and VKM (2016), may be considered.

#### Planned approach towards the evidence retrieval from the scientific literature

The following sections will summarise the approach taken for the evidence retrieval to answer the predefined subquestions (Section 1.1).

Linoleic acid and alpha-linolenic acid concentrations in adipose tissue and their release from adipose tissue during weight loss

References for these two questions will be screened jointly (to limit duplicates; Q1).

#### Eligible studies are:

Human intervention (clinical trials) or observational studies in adults not on an intentionally modified diet (irrespective of weight status) on the FA composition of human AT or FA release from human AT:

- Studies in study populations living in Europe.
- Studies in either healthy subjects or in overweight or obese individuals with hypertension, hyperlipidaemia or T2DM, but no other disease. Medication use should be restricted to medicines related to these diseases.
- At title and abstract screening,
  - studies on FA composition of subcutaneous (SC) AT in which samples were taken by biopsies or from visceral (VC) AT taken during surgery or autopsy (incl. subsequent gas chromatography or other methods of sample analysis),
  - or studies on FA composition of SC AT before and after weight loss,
  - or studies on FA release during weight loss or in the fasting state via microdialysis of the tissue of interest or using isotopes to study the fate of the FA in metabolism.
- To be finally included,

articles providing quantitative data on LA (18:2 (n-6)) and/or ALA (18:3 (n-3)) concentration of AT. Preferably, full-text papers should report on the study population characteristics (including age, sex), diet, weight and health status to be included. For large observational studies, this information may be provided in other publications on the same studies.

#### Not eligible are:

- Systematic or narrative reviews and meta-analyses. Although these may be used to provide background information to the general sections of the statement or for hand search of relevant references.
- Protocols (as no results are reported), commentaries, editorials, letters to the editor, grey literature (PhD theses, extended abstracts, conference proceedings, etc.), or other publication types not peer-reviewed (except contributions from stakeholders and interested parties).
- Animal studies, *in vitro* studies and studies on cells.
- Studies on infants, children and adolescents, pregnant and lactating women.
- Studies on patients except for diseases listed above, as they may have an impact on the outcome of interest,
- Studies on subjects on medication except related to the diseases listed above.
- Studies on dietary FA/FA intake only.
- Studies on FA concentration not measured in AT, e.g. in liver, muscle, brain, bone marrow, etc.
- Studies on plasma free FA only.
- Studies on individuals living outside of Europe.
- Additional reasons at full-text screening:
  - studies not reporting on LA and/ALA quantitatively in SC AT or VC AT.
  - inappropriate method of measurement.

Range of weight loss when consuming TDR

#### Eligible studies are:

Human intervention studies (i.e. clinical trials, including single arm trials) in overweight or obese<sup>8</sup> adults, in which TDRs with an energy content between 600 and 1,200 kcal (i.e. 2,510–5,020 kJ/day) are administered (i.e. within the permitted range as laid down in Commission delegated Regulation (EU)  $2017/1798^{1}$ ) and that report on weight loss (Q2):

- As the terms 'total diet replacement' are rarely present in the abstracts, studies on 'total meal replacement', 'very low calorie diet' or 'low calorie diet' will be included at title and abstract screening if the diet investigated is in the energy range as specified in the Regulation.
- TDRs may have been consumed with or without added/supplemental vitamins and/or minerals (considering vitamins and/or minerals will not have an impact on weight loss).
- TDRs could have been consumed before bariatric surgery.
- Overweight or obese subjects without apparent co-morbidity, or with hypertension, hyperlipidaemia, T2DM, but no other disease. Medication use should be restricted to medicines related to the disease listed.
- For practical reasons during the title and abstract screening, as the abstracts often do not provide information in a harmonised and/or detailed way, the following criteria will be applied:
  - the maximal duration of the studies included at title and abstract level should be less than 6 months (no minimal duration expected).
  - abstracts of studies only mentioning the daily energy restriction/deficit (compared to the initial diet) will be included for full-text screening if this deficit is of at least -800 kcal/day (-3,347 kJ/day), is expressed in absolute amount, or at least -40% energy/day if expressed as a percentage.
  - if the abstracts report the energy intake per kg body weight, the 'rule of thumb' to decide if the inclusion or exclusion at the next step is to multiply by 60 kg to calculate the calories/day.
- For full-text screening, additional criteria are:



- studies in which body weight (or fat mass) is measured by investigators (i.e. no self-reported body weight) using validated and standardised methods, before and immediately after energy restriction.
- studies that report on the amount of weight loss, the caloric content of the TDR administered and the duration of the energy restriction.
- studies that report on weight loss up to and including 2 months.
- studies that report on compliance and how compliance was assessed.

Preferably, full-text publications included at title and abstract screening should report on the study population characteristics (including age, sex), diet, weight and health status.

#### Not eligible are:

- Studies on weight loss following diets not based on specifically designed foods, e.g. Atkins, DASH,<sup>14</sup> Paleolithic, Mediterranean, 'low carb', 'low fat', vegetarian, ketogenic (if not with specially designed foods), low glycaemic diet (if not with specially designed foods/TDR) or 'low calorie'/'low energy'/'hypocaloric'/'energy-restricted' diets using usual foods e.g. almonds, dairy, liquorice.
- Studies on intermittent fasting.
- Studies undertaken after bariatric surgery.
- Studies on subjects with catabolic diseases (such as cancer) should be excluded, as these diseases may have an impact on the outcome of interest).
- Studies in which TDR/energy-restricted diets was consumed in combination with a medication for weight loss in all groups or with training/physical activity/exercise, or counselling/group sessions or with other foods (even if in limited amounts) in all groups (i.e. no arm with TDR/ energy-restricted diet and without co-intervention).
- Observational studies (e.g. surveys, case reports, case-series, prospective cohort, case-control, retrospective).
- Systematic or narrative reviews and meta-analyses. Although, these may be used to provide background information to the general sections of the statement or for hand search of relevant references.
- Protocols (as no results are reported), commentaries, editorials, letters to the editor, grey literature (PhD theses, extended abstracts, conference proceedings, etc.), or other publication types not peer-reviewed except contributions from stakeholders and interested parties.
- Studies on infants, children and adolescents, pregnant and lactating women, normal weight/ lean subjects (i.e. BMI below 25).
- Animal studies, *in vitro* studies.
- Studies on meal replacements (also called 'partial meal replacement'), as these are not covered by Commission delegated Regulation (EU) 2017/1798 and Regulation (EU) 609/2013.
- Studies not using a specifically formulated product (i.e. TDRs) or products with an energy content outside the range as specified in the Regulation.

#### Magnesium and risk of developing diarrhoea

### Eligible studies are:

Human intervention studies (clinical trials) that report on the risk of developing diarrhoea associated with supplemental Mg or Mg intentionally added to food in adults (Q3):

- The intervention studies should have at least two arms and compare different levels of supplemental/added Mg (possibly including a placebo) administered orally to adults.
- Trials in which <u>only</u> the amount of Mg consumed between groups differ.
- Studies in subjects either healthy or defined as overweight/obese presenting with hypertension, hyperlipidaemia or T2DM.
- Studies reporting on adverse effects (including diarrhoea) associated with Mg administration. Studies included at title and abstract level may report on adverse effects only at full-text level. Studies for which the full texts report on various adverse effects but not diarrhoea will be also considered as relevant for inclusion.

<sup>&</sup>lt;sup>14</sup> Dietary Approaches to Stop Hypertension.



- Studies that report on the definition of diarrhoea (applying the World Health Organization (WHO) criteria). For the full-text screening, trials reporting on Mg administration and (the severity of) diarrhoea should preferably report on the frequency and consistency of the stools using validated assessment methods and documenting diarrhoea by the frequency of  $\geq$  3 loose or watery stools per day.<sup>11</sup> Hence, a ranking of the final included studies may be made, distinguishing those with a reliable outcome assessment from those with an unreliable outcome assessment or improper reporting.
- After full-text screening, included studies should specify (among other parameters) the Mg dose and duration of administration in all groups.

#### Not eligible are:

- Systematic or narrative reviews and meta-analyses. However, these may be used to provide background information to the general sections of the statement or for hand search of relevant references.
- Observational studies, animal studies, *in vitro* studies, studies in cells, protocols (as no results are reported), commentaries, editorials, letters to the editor, grey literature (PhD theses, extended abstracts, conference proceedings, etc.), or other publication types not peer-reviewed except contributions from stakeholders and interested parties.
- Studies in infants, children and adolescents, pregnant and lactating women, patients with diseases not mentioned above.
- Studies comparing similar doses of different forms of Mg.
- Single arm studies.
- Studies that investigate the effect of Mg in combination with other substances
- Studies on Mg naturally present in food, as the UL for Mg set by SCF only applies to readily dissociable Mg salts.
- Studies in which Mg is not provided orally (e.g. injection, perfusion, infusion, nebulisation, intramuscular, intrathecal, intravenous or intraperitoneal administration, transdermal administration, bioresorbable devices, placental transfer), including those with an initial parenteral Mg administration.
- Studies not on the subject of interest, e.g. on Mg content of foods or breast milk, on Mg deficiency/insufficiency/hypomagnesaemia, or on Mg status/biomarkers/adequacy.
- At full-text screening, publications not reporting on the Mg dose and duration of consumption.
- At full-text screening, publications not reporting on adverse events.

Dietary fat and risk of gallstone formation

#### Eligible studies are:

Human intervention studies investigating the relationship between low-fat energy-restricted diets and the risk of gallstone/biliary sludge formation or gallbladder emptying (Q4):

- Studies published from the year 2014 and onwards, i.e. starting from the conclusion of the scientific assessment by EFSA NDA Panel (2015b).
- Human intervention studies in adults comparing at least two different fat contents of energyrestricted diets or investigating the effect of at least two test meals with varying fat content (on gallbladder emptying).
- Studies that report on the fat and caloric content of the diet per day and the duration of the dietary intake.
- Studies reporting on gallstone formation or biliary sludge formation or gallbladder emptying.

Preferably, full-text papers of studies included at title and abstract screening should report on the study population characteristics (including age, sex), diet, weight and health status to be included.

#### Not eligible are:

- Systematic or narrative reviews and meta-analyses. Although these may be used to provide background information to the general sections of the statement or for hand search of relevant references.
- Observational studies, animal studies, *in vitro* studies, protocols (as no results are reported), commentaries, editorials, letters to the editor, or other publication types not peer-reviewed,



grey literature (PhD theses, extended abstracts, conference proceedings, etc.) except contributions from stakeholders and interested parties.

• Studies on infants, children and adolescents, pregnant and lactating women and studies on patients with diseases not listed above.

#### Method for data extraction from included studies

Data will be extracted in prespecified forms in Microsoft Excel<sup>®</sup> by one reviewer and a second reviewer will serve as validator. The data extraction will be divided according to the main literature searches, i.e. LA and ALA concentration of and release from human adipose tissue during weight loss (Q1), range of weight loss when consuming TDRs (Q2), Mg administration and risk of diarrhoea (Q3) and dietary fat and risk of gallstone formation (Q4). Missing data will only be collected by contacting corresponding authors in cases where clarification is critical for the interpretation of results or for the decision to include a study.

#### Method for appraising evidence

Appraisal of included studies is not foreseen.

#### Preliminary identification of sources of uncertainty and methods for prioritising them

Uncertainty analysis of the scientific assessment, i.e. identifying possible limitations in scientific knowledge and assessing their implications for scientific conclusions, will be discussed briefly, based on the EFSA guidance document on uncertainty (EFSA Scientific Committee, 2018). This implies, in particular, identifying the sources of uncertainty affecting the assessment, prioritising these sources based on their expected influence on the outcome/results and final overall discussions and planning how the uncertainty analysis will be handled. It is expected that the following identified sources of uncertainties will be discussed qualitatively (descriptive method) and no quantitative analysis will be undertaken.

The following uncertainties have been preliminary identified:

- Uncertainty in the method and precision of measurement.
- Exposure/compliance to TDR regimen/to Mg consumption.
- Reporting/assessment of the adverse effect 'diarrhoea' by investigators
- Publication bias.
- Language (only English language considered).
- Representativity/relevance for the EU population.

Uncertainties will be assessed by expert judgement.

#### Methods for analysing uncertainties individually and combined

Uncertainties will be identified at each step of the assessment, but no formal uncertainty assessment is foreseen.

#### Methods for synthesising evidence

The method for synthesising the evidence for points A–E (Section 1.2 of the statement) will be primarily semiquantitative.

A qualitative approach will be followed for those subquestions belonging to point A (Section 1.2 of the statement) answering to the influence of the methods of measurement and the extent of reutilisation of LA and ALA upon release from AT.

A conservative approach will be taken when assessing the evidence to cover the entire population that could potentially consume TDRs.

Expert knowledge elicitation (EKE) might be needed, taking into account the relevant EFSA guidance (EFSA, 2014),<sup>15</sup> if updated composition requirements for ALA, LA and Mg are set.

<sup>&</sup>lt;sup>15</sup> http://www.efsa.europa.eu/en/efsajournal/pub/3734



### Appendix E – Search strings

# E.1. Linoleic acid and alpha-linolenic acid concentrations in adipose tissue and their release from adipose tissue (Q1)

#### Date of search: 8 June 2020

### Linoleic acid and alpha-linolenic acid concentrations in adipose tissue Embase

Search	Query	Items identified
#8	#6 NOT #7	3,690
#7	#3 AND #4 AND ([editorial]/lim OR [letter]/lim)	16
#6	#5 AND [humans]/lim AND [english]/lim	3,704
#5	#3 AND #4	10,416
#4	#1 OR #2	85,376
#3	'adipose tissue/exp OR 'adipose tissue cell'/exp OR adipocyte*:ti,ab,kw OR (((adipose OR fat OR fatty) NEAR/3 (tissue* OR body)):ti,ab,kw) OR ((fat NEAR/3 (abdominal OR cell OR cells OR intraabdominal OR pad OR pads OR subcutaneous OR visceral)):ti,ab,kw)	285,640
#2	('fatty acid'/de OR 'essential fatty acid'/exp OR 'unsaturated fatty acid'/exp OR ffa:ti,ab, kw OR ffa:ti,ab,kw OR efa:ti,ab,kw OR efas:ti,ab,kw OR pufa:ti,ab,kw OR pufa:ti,ab,kw OR ufa:ti,ab,kw OR ufa:ti,ab,kw OR ((fatty OR 'alpha linolenic' OR alphalinolenic OR linolic OR linoleicOR 'n 3' OR 'n 6') NEAR/3 (acid OR acids)) OR linolate:ti,ab,kw OR linoleate:ti,ab,kw OR linolenate:ti,ab,kw OR 'omega 3':ti,ab,kw OR 'omega 6':ti,ab,kw OR omega3:ti,ab,kw OR omega6:ti,ab,kw OR $\omega$ 3:ti,ab,kw OR $\omega$ 6:ti,ab,kw OR '18 $3\omega$ 3':ti,ab,kw OR '183omega3':ti,ab,kw OR '18 3omega3':ti,ab,kw) AND 'lipid composition'/exp	19,889
#1	((ffa OR ffas OR efa OR efas OR pufa OR pufas OR ufa OR ufas OR 'fatty acid' OR 'fatty acids' OR 'alpha linolenic acids' OR 'alpha linolenic acids' OR 'alpha linolenic acids' OR 'alpha linolenic acids' OR 'linoleic acids' OR 'linolic acids' OR 'linolic acids' OR 'linolic acids' OR 'linolete OR linoleate OR linoleate OR 'n 3 acid' OR 'n 3 acids' OR 'n 6 acid' OR 'n 6 acid' OR 'n 6 acid' OR 'n 6 acids' OR '18 3000  OR '18 3000 OR '18 30000 OR '18 3000000000000000000000000000000000000	78,162

#### PubMed

Search	Query	Items identified
#13	Search: (((((Amount[tiab] OR biops*[tiab] OR composition[tiab] OR concentration*[tiab] OR constituent[tiab] OR content*[tiab] OR distribution*[tiab] OR level[tiab] OR levels [tiab] OR pattern*[tiab] OR percentage*[tiab] OR profile[tiab]) AND ("Fatty Acids"[Mesh: NoExp] OR "Fatty Acids, Unsaturated"[Mesh] OR "Fatty Acids, Essential"[Mesh] OR Fatty acid[tiab] OR fatty acids[tiab] OR FFA[tiab] OR FFAs[tiab] OR EFAs[tiab] OR EFAs[tiab] OR PUFA[tiab] OR PUFAs[tiab] OR UFAs[tiab] OR UFAs[tiab] OR Alpha linolenic acid[tiab] OR Alpha linolenic acid[tiab] OR Alpha linolenic acids[tiab] OR Alphalinolenic acid[tiab] OR Linoleic acids[tiab] OR Linoleic acids[tiab] OR Linoleic acids[tiab] OR Linoleic acids[tiab] OR ND ("n 3"[tiab] OR "n 6"[tiab]) AND (acid [tiab] OR acids[tiab]) OR 0mega6[tiab] OR ("n 3"[tiab] OR "n 6"[tiab]) AND (acid [tiab] OR acids[tiab]) OR $\infty 3$ [tiab] OR $\infty 6$ [tiab]) AND ("Adiposity"[Mesh] OR "Adipose Tissue"[Mesh] OR "Adipocytes"[Mesh] OR Body fat[tiab] OR Fat cell[tiab] OR Fat pads[tiab] OR Body fat[tiab] OR Fat tissue*[tiab] OR Fat cell[tiab] OR Fat pads[tiab] OR Subcutaneous fat[tiab] OR Visceral fat[tiab]) NOT	6,512



Search	Query	Items identified
	(('Animals"[Mesh] NOT ('Animals"[Mesh] AND "Humans"[Mesh])))) NOT ((rat[ti] OR rats [ti] OR mouse[ti] OR mice[ti] OR swine[ti] OR porcine[ti] OR murine[ti] OR sheep[ti] OR lambs[ti] OR pigs[ti] OR piglets[ti] OR rabbit[ti] OR rabbits[ti] OR cat[ti] OR cats[ti] OR dog[ti] OR dogs[ti] OR cattle[ti] OR bovine[ti] OR monkey[ti] OR monkeys[ti] OR trout[ti] OR marmoset*[ti]))) AND ("english"[Language])) NOT (("editorial"[Publication Type]) OR ("letter"[Publication Type])) Sort by: Most Recent	
#12	Search: ("editorial"[Publication Type]) OR ("letter"[Publication Type]) Sort by: Most Recent	1,610,464
#11	Search: (((((Amount[tiab] OR biops*[tiab] OR composition[tiab] OR concentration*[tiab] OR constituent[tiab] OR content*[tiab] OR distribution*[tiab] OR level[tiab] OR levels [tiab] OR pattern*[tiab] OR percentage*[tiab] OR profile[tiab]) AND ("Fatty Acids"[Mesh: NoExp] OR "Fatty Acids, Unsaturated"[Mesh] OR "Fatty Acids, Essential"[Mesh] OR Fatty acid[tiab] OR fatty acids[tiab] OR FFA[tiab] OR "FAs[tiab] OR EFAs[tiab] OR EFAs[tiab] OR PUFA[tiab] OR PUFAs[tiab] OR UFA[tiab] OR UFAs[tiab] OR Alpha linolenic acid[tiab] OR Alpha linolenic acids[tiab] OR UFA[tiab] OR UFAs[tiab] OR Alpha linolenic acids[tiab] OR Linoleic acid[tiab] OR Linoleic acids[tiab] OR Linolic acids[tiab] OR linolate[tiab] OR linoleate[tiab] OR Linolenate[tiab] OR "omega 3"[tiab] OR "omega 6"[tiab] OR omega3[tiab] OR omega6[tiab] OR (("n 3"[tiab] OR "n 6"[tiab]) AND (acid [tiab] OR acids[tiab])) OR "183ω3"[tiab] OR "18 3ω3"[tiab] OR "1830mega3"[tiab] OR "18 30mega3"[tiab] OR ω3[tiab] OR ω6[tiab])) AND ("Adiposity"[Mesh] OR "Adipose Tissue"[Mesh] OR "Adipocytes"[Mesh] OR adipocyte*[tiab] OR Fat cell[tiab] OR Fat cells[tiab] OR Fat pad[tiab] OR Fat pads[tiab] OR Fat tissue*[tiab] OR Fat cells[tiab] OR Fat pad[tiab] OR Subcutaneous fat[tiab] OR Visceral fat[tiab]) NOT (("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))) NOT ((rat[ti] OR rats [ti] OR mouse[ti] OR mice[ti] OR swine[ti] OR porcine[ti] OR murine[ti] OR sheep[ti] OR lambs[ti] OR pigs[ti] OR cattle[ti] OR swine[ti] OR rabits[ti] OR cat[ti] OR trout[ti] OR marmoset*[ti])) AND ("english"[Language]) Sort by: Most Recent	6,532
#10	Search: "english"[Language] Sort by: Most Recent	26,364,599
#9	Search: ((((Amount[tiab] OR biops*[tiab] OR composition[tiab] OR concentration*[tiab] OR constituent[tiab] OR content*[tiab] OR distribution*[tiab] OR level[tiab] OR levels [tiab] OR pattern*[tiab] OR percentage*[tiab] OR profile[tiab]) AND ("Fatty Acids"[Mesh: NoExp] OR "Fatty Acids, Unsaturated"[Mesh] OR "Fatty Acids, Essential"[Mesh] OR Fatty acid[tiab] OR fatty acids[tiab] OR FFA[tiab] OR "FAs[tiab] OR EFAs[tiab] OR EFAs[tiab] OR PUFA[tiab] OR PUFAs[tiab] OR UFA[tiab] OR UFAs[tiab] OR Alpha linolenic acid[tiab] OR Alpha linolenic acids[tiab] OR UFA[tiab] OR UFAs[tiab] OR Alpha linolenic acids[tiab] OR Linoleic acid[tiab] OR Linoleic acids[tiab] OR Linolic acids[tiab] OR linolate[tiab] OR linoleate[tiab] OR Linolenate[tiab] OR "omega 3"[tiab] OR "omega 6"[tiab] OR omega3[tiab] OR omega6[tiab] OR (("n 3"[tiab] OR "n 6"[tiab]) AND (acid [tiab] OR acids[tiab])) OR "183 $\omega$ 3"[tiab] OR "18 3 $\omega$ 3"[tiab] OR "1830mega3"[tiab] OR "18 30mega3"[tiab] OR $\omega$ 6[tiab])) AND ("Adiposity"[Mesh] OR "Adipose Tissue"[Mesh] OR "Adipocytes"[Mesh] OR adipocyte*[tiab] OR Fat cell[tiab] OR Fat cells[tiab] OR Fat pad[tiab] OR Fat pads[tiab] OR Fat tissue*[tiab] OR Fat cells[tiab] OR Fat pad[tiab] OR Subcutaneous fat[tiab] OR Visceral fat[tiab] OR Fat tiab] OR mouse[ti] OR mice[ti] OR swine[ti] OR porcine[ti] OR murine[ti] OR sheep[ti] OR lambs[ti] OR pigs[ti] OR mice[ti] OR swine[ti] OR rabbit[ti] OR murine[ti] OR cats[ti] OR lambs[ti] OR pigs[ti] OR cattle[ti] OR bovine[ti] OR monkey[ti] OR monkeys[ti] OR trout[ti] OR marmoset*[ti])) Sort by: Most Recent	6,828
#8	Search: (rat[ti] OR rats[ti] OR mouse[ti] OR mice[ti] OR swine[ti] OR porcine[ti] OR murine[ti] OR sheep[ti] OR lambs[ti] OR pigs[ti] OR piglets[ti] OR rabbit[ti] OR rabbits[ti] OR cat[ti] OR cats[ti] OR dog[ti] OR dogs[ti] OR cattle[ti] OR bovine[ti] OR monkey[ti] OR monkeys[ti] OR trout[ti] OR marmoset*[ti]) Sort by: Most Recent	2,007,584



Search	Query	Items identified
#7	Search: (((Amount[tiab] OR biops*[tiab] OR composition[tiab] OR concentration*[tiab] OR constituent[tiab] OR content*[tiab] OR distribution*[tiab] OR level[tiab] OR levels [tiab] OR pattern*[tiab] OR percentage*[tiab] OR profile[tiab]) AND ("Fatty Acids"[Mesh: NoExp] OR "Fatty Acids, Unsaturated"[Mesh] OR "Fatty Acids, Essential"[Mesh] OR Fatty acid[tiab] OR fatty acids[tiab] OR FFA[tiab] OR FFAs[tiab] OR EFAs[tiab] OR EFAs[tiab] OR PUFA[tiab] OR PUFAs[tiab] OR UFAs[tiab] OR UFAs[tiab] OR Alpha linolenic acid[tiab] OR Alpha linolenic acids[tiab] OR Alpha linolenic acids[tiab] OR Alphalinolenic acid[tiab] OR Linoleic acids[tiab] OR Linoleic acids[tiab] OR Linoleic acids[tiab] OR Linoleic acids[tiab] OR linolate[tiab] OR linoleate[tiab] OR Linolenate[tiab] OR "n 6"[tiab] OR "omega 6"[tiab] OR acids[tiab] OR omega6[tiab] OR (("n 3"[tiab] OR "n 6"[tiab]) AND (acid [tiab] OR acids[tiab] OR $\omega$ 3[tiab] OR $\omega$ 6[tiab])) AND ("Adipose tissue*[tiab] OR "Adipose tissue*[tiab] OR Adipose body[tiab] OR Abdominal fat[tiab] OR Body fat[tiab] OR Fat cell[tiab] OR Fat cells[tiab] OR Fat pads[tiab] OR Body fat[tiab] OR Fat cell[tiab] OR Fat cells[tiab] OR Fat pads[tiab] OR Subcutaneous fat[tiab] OR Visceral fat[tiab]) NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))) Sort by: Most Recent	7,767
#6	Search: (``Animals"[Mesh] NOT (``Animals"[Mesh] AND ``Humans"[Mesh])) Sort by: Most Recent	4,705,782
#5	Search: ((Amount[tiab] OR biops*[tiab] OR composition[tiab] OR concentration*[tiab] OR constituent[tiab] OR content*[tiab] OR distribution*[tiab] OR level[tiab] OR levels[tiab] OR pattern*[tiab] OR percentage*[tiab] OR profile[tiab]) AND ("Fatty Acids"[Mesh: NoExp] OR "Fatty Acids, Unsaturated"[Mesh] OR "Fatty Acids, Essential"[Mesh] OR Fatty acid[tiab] OR fatty acids[tiab] OR FFA[tiab] OR "Fatty Acids, Essential"[Mesh] OR FAs[tiab] OR PUFA[tiab] OR fatty acids[tiab] OR FFA[tiab] OR UFAs[tiab] OR EFAs[tiab] OR EFAs[tiab] OR PUFA[tiab] OR PUFAs[tiab] OR UFAs[tiab] OR UFAs[tiab] OR Alpha linolenic acid[tiab] OR Alpha linolenic acids[tiab] OR Alpha linolenic acids[tiab] OR Linoleic acids[tiab] OR Linoleic acids[tiab] OR Linoleic acids[tiab] OR Linoleic acids[tiab] OR linolate[tiab] OR Linoleate[tiab] OR Linoleate[tiab] OR Nomega 3"[tiab] OR "omega 6"[tiab] OR omega3[tiab] OR omega6[tiab] OR (("n 3"[tiab] OR "1830mega3"[tiab] OR "1830mega3"[tiab] OR "18 30mega3"[tiab] OR "30mega3"[tiab] OR modeltab])) AND ("Adipose tissue*[tiab] OR "Adipose body[tiab] OR Adipose tissue*[tiab] OR Body fat[tiab] OR Fat cell[tiab] OR Fat cell[tiab] OR Fat pads[tiab] OR Fat tissue*[tiab] OR Fatty acids[tiab] OR Fat pads[tiab] OR Fat tissue*[tiab] OR Fatty acids[tiab] OR Intraabdominal fat[tiab] OR Subcutaneous fat[tiab] OR Visceral fat[tiab) Sort by: Most Recent	16,638
#4	Search: "Adiposity" [Mesh] OR "Adipose Tissue" [Mesh] OR "Adipocytes" [Mesh] OR adipocyte* [tiab] OR Adipose tissue* [tiab] OR Adipose body [tiab] OR Abdominal fat[tiab] OR Body fat[tiab] OR Fat cell[tiab] OR Fat cells[tiab] OR Fat pad[tiab] OR Fat pads[tiab] OR Fat tissue* [tiab] OR Fatty tissue* [tiab] OR Intraabdominal fat[tiab] OR Subcutaneous fat[tiab] OR Visceral fat[tiab] Sort by: Most Recent	193,456
#3	Search: "Fatty Acids" [Mesh:NoExp] OR "Fatty Acids, Unsaturated" [Mesh] OR "Fatty Acids, Essential" [Mesh] OR Fatty acid[tiab] OR fatty acids[tiab] OR FFA[tiab] OR FFAs[tiab] OR EFA[tiab] OR EFAs[tiab] OR PUFA[tiab] OR PUFAs[tiab] OR UFAs[tiab] OR Alpha linolenic acid[tiab] OR Alpha linolenic acids[tiab] OR Alphalinolenic acid[tiab] OR Alphalinolenic acids[tiab] OR Linoleic acid[tiab] OR Linoleic acids[tiab] OR Linolic acids[tiab] OR Linoleic acid[tiab] OR Linoleic acids[tiab] OR [tiab] OR Linolic acids[tiab] OR linolate[tiab] OR linoleate[tiab] OR Linolenate[tiab] OR "omega 3"[tiab] OR "omega 6"[tiab] OR omega3[tiab] OR omega6[tiab] OR (("n 3"[tiab] OR "n 6"[tiab]) AND (acid[tiab] OR acids[tiab])) OR "183 $\omega$ 3"[tiab] OR "18 3 $\omega$ 3"[tiab] OR "183omega3"[tiab] OR "18 3omega3"[tiab] OR $\omega$ 6[tiab] Sort by: Most Recent	434,755
#2	Search: Amount[tiab] OR biops*[tiab] OR composition[tiab] OR concentration*[tiab] OR constituent[tiab] OR content*[tiab] OR distribution*[tiab] OR level[tiab] OR levels[tiab] OR pattern*[tiab] OR percentage*[tiab] OR profile[tiab] Sort by: Most Recent	8,394,012
#18	#8 AND #16 AND [english]/lim	1,764
#17	#8 AND #16	1,806
#16	#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15	5,460,152



Search	Query	Items identified
#15	((data NEAR/1 (synthes* OR extraction* OR abstraction*)):ti,ab) OR handsearch*:ti,ab OR 'hand search':ti,ab OR 'hand searches':ti,ab OR 'hand searching':ti,ab OR 'mantel haenszel':ti,ab OR peto:ti,ab OR 'der simonian':ti,ab OR dersimonian:ti,ab OR 'fixed effect':ti,ab OR 'fixed effects':ti,ab OR 'latin square':ti,ab OR 'latin squares':ti,ab OR 'meta analysis':ti,ab OR 'meta analyses':ti,ab OR 'met analysis':ti,ab OR 'meta analysis':ti,ab OR metanaly*:ti,ab OR 'meta regression':ti,ab OR 'meta regressions':ti,ab OR metanegression*:ti,ab OR medline:ti,ab OR cochrane:ti,ab OR pubmed:ti,ab OR medlars:ti,ab OR embase:ti,ab OR cinahl:ti,ab OR cochrane:jt OR 'evidence report':jt OR ((comparative NEAR/3 (efficacy OR effectiveness)):ti,ab) OR 'outcomes research':ti,ab OR 'relative effectiveness':ti,ab OR (((indirect OR 'indirect treatment' OR 'mixed treatment') NEAR/3 comparison):ti,ab)	457,229
#14	((systematic* NEAR/3 (review* OR overview*)):ti,ab) OR ((methodologic* NEAR/3 (review* OR overview*)):ti,ab) OR ((quantitative NEAR/3 (review* OR overview* OR synthes*)):ti,ab) OR ((research NEAR/3 (integrati* OR overview*)):ti,ab) OR ((integrative NEAR/3 (review* OR overview*)):ti,ab) OR ((collaborative NEAR/3 (review* OR overview*)):ti,ab) OR ((pool* NEAR/3 analy*):ti, ab)	273,284
#13	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR 'systematic review'/exp OR 'systematic review (topic)'/exp OR 'biomedical technology assessment'/exp	402,070
#12	<pre>`crossover procedure'/exp OR (((crossover OR 'cross over') NEAR/10 (study OR studies OR design* OR method* OR procedure OR comparison)):ti,ab)</pre>	93,441
#11	((singl* OR doubl* OR trebl* OR tripl*) NEAR/10 (mask* OR blind* OR dumm*)):ti,ab	249,336
#10	'clinical trial (topic)'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'triple blind procedure'/exp	532,576
#9	'clinical trial'/exp OR 'randomization'/exp OR randomized:ti,ab OR randomised:ti,ab OR placebo:ti,ab OR randomly:ti,ab OR trial:ti,ab OR groups:ti,ab OR ('group 1':ti,ab,kw AND 'group 2':ti,ab,kw)	4,883,034
#8	#6 NOT #7	5,091
#7	(rat:ti OR rats:ti OR mouse:ti OR mice:ti OR swine:ti OR porcine:ti OR murine:ti OR sheep:ti OR lambs:ti OR pigs:ti OR piglets:ti OR rabbit:ti OR rabbits:ti OR cat:ti OR cats:ti OR dog:ti OR dogs:ti OR cattle:ti OR bovine:ti OR monkey:ti OR monkey:ti OR trout:ti OR marmoset*:ti) AND 'animal experiment'/de	1,064,962
#6	#4 NOT #5	5,185
#5	'animal experiment'/de NOT ('human experiment'/de OR 'human'/de)	2,250,451
#4	#1 AND #2 AND #3	8,320
#3	'body weight change'/exp OR (((weight OR fat OR 'adipose tissue') NEAR/3 (decreas* OR loss OR losing OR reduc*)):ti,ab,kw) OR ((weightNEAR/3 management):ti, ab,kw) OR ((chang* NEAR/3 ('adipose tissue' OR 'fat mass' OR 'fat tissue' OR weight)):ti, ab,kw)	419,800
#2	'fatty acid'/de OR 'essential fatty acid'/exp OR 'unsaturated fatty acid'/exp OR ffa:ti,ab,kw OR ffa:ti,ab,kw OR efa:ti,ab,kw OR efa:ti,ab,kw OR pufa:ti,ab,kw OR pufa:ti,ab,kw OR ufa:ti,ab,kw OR ufa:ti,ab,kw OR ((fatty OR 'alpha linolenic' OR alphalinolenic OR linolic OR linoleicOR 'n 3' OR 'n 6') NEAR/3 (acid OR acids)) OR linolate:ti,ab,kw OR linoleate:ti,ab,kw OR linolenate:ti,ab,kw OR 'omega 3':ti,ab,kw OR 'omega 6':ti,ab,kw OR omega3:ti,ab,kw OR omega6:ti,ab,kw OR \u03b2 ti,ab,kw OR \u03b2 ti,ab,kw OR '18 3\u03b2':ti,ab,kw OR '1830mega3':ti,ab,kw OR '18 30mega3':ti,ab,kw	423,778
#1	'adipose tissue'/exp OR 'adipose tissue cell'/exp OR adipocyte*:ti,ab,kw OR (((adipose OR fat OR fatty) NEAR/3 (tissue* OR body)):ti,ab,kw) OR ((fat NEAR/3 (abdominal OR cell OR cells OR intraabdominal OR pad OR pads OR subcutaneous OR visceral)):ti,ab,kw)	285,922



#### PubMed

Search	Query	Items identified
#14	Search: "english"[Language] AND #13 Sort by: Most Recent	1,356
#13	Search: #12 AND #9 Sort by: Most Recent	1,387
#12	Search: #10 OR #11 Sort by: Most Recent	3,747,938
#11	Search: systematic[sb] OR meta-analysis[pt] OR meta-analysis as topic[Mesh] OR meta- analysis[Mesh] OR meta analy*[tw] OR metanaly*[tw] OR metaanaly*[tw] OR meta analy*[tw] OR integrative research[tiab] OR integrative review*[tiab] OR integrative overview*[tiab] OR research integration*[tiab] OR research overview*[tiab] OR collaborative review*[tiab] OR collaborative overview*[tiab] OR systematic review*[tiab] OR comparative efficacy[tiab] OR comparative effectiveness[tiab] OR outcomes research [tiab] OR indirect comparison*[tiab] OR Embase*[tiab] OR Cinahl*[tiab] OR systematic overview*[tiab] OR methodological overview*[tiab] OR methodologic overview*[tiab] OR methodological review*[tiab] OR methodologic review*[tiab] OR quantitative review* [tiab] OR quantitative overview*[tiab] OR quantitative synthes*[tiab] OR pooled analy* [tiab] OR Cochrane[tiab] OR Medline[tiab] OR Pubmed[tiab] OR Medlars[tiab] OR handsearch*[tiab] OR hand search*[tiab] OR meta-regression*[tiab] OR metaregression* [tiab] OR data synthes*[tiab] OR data extraction[tiab] OR data abstraction*[tiab] OR mantel haenszel[tiab] OR peto[tiab] OR der-simonian[tiab] OR dersimonian[tiab] OR fixed effect*[tiab] OR "Cochrane Database Syst Rev"[Journal:jrid21711] Sort by: Most Recent	421,910
#10	Search: "clinical trial"[pt] OR "Random Allocation"[Mesh] OR randomized[tiab] OR randomised[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR ("group 1"[tiab] AND "group 2"[tiab]) OR "Clinical Trials as Topic"[Mesh] OR "Double- Blind Method"[Mesh] OR "Single-Blind Method"[Mesh] OR ((singl*[tiab] OR doubl*[tiab] OR trebl*[tiab] OR tripl*[tiab]) AND (mask*[tiab] OR blind*[tiab] OR dumm*[tiab])) OR "Cross-Over Studies"[Mesh] OR ((crossover[tiab] OR "cross over"[tiab]) AND (study[tiab] OR studies[tiab] OR design*[tiab] OR method*[tiab] OR procedure[tiab] OR comparison [tiab])) Sort by: Most Recent	3,484,152
#9	Search: #7 NOT #8 Sort by: Most Recent	4,775
#8	Search: (rat[ti] OR rats[ti] OR mouse[ti] OR mice[ti] OR swine[ti] OR porcine[ti] OR murine[ti] OR sheep[ti] OR lambs[ti] OR pigs[ti] OR piglets[ti] OR rabbit[ti] OR rabbits[ti] OR cat[ti] OR cats[ti] OR dog[ti] OR dogs[ti] OR cattle[ti] OR bovine[ti] OR monkey[ti] OR monkeys[ti] OR trout[ti] OR marmoset*[ti]) Sort by: Most Recent	2,010,568
#7	Search: #5 NOT #6 Sort by: Most Recent	5,629
#6	Search: ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) Sort by: Most Recent	4,711,847
#5	Search: #1 AND #3 AND #4 Sort by: Most Recent	12,817
#4	Search: "Fatty Acids" [Mesh:NoExp] OR "Fatty Acids, Unsaturated" [Mesh] OR "Fatty Acids, Essential" [Mesh] OR Fatty acid[tiab] OR fatty acids[tiab] OR FFA[tiab] OR FFAs[tiab] OR EFA[tiab] OR EFAs[tiab] OR PUFA[tiab] OR PUFAs[tiab] OR UFAs[tiab] OR UFAs[tiab] OR Alpha linolenic acid[tiab] OR Alpha linolenic acids[tiab] OR Alphalinolenic acid[tiab] OR Alphalinolenic acids[tiab] OR Linoleic acid[tiab] OR Linoleic acids[tiab] OR Linolic acid [tiab] OR Linolic acids[tiab] OR linolate[tiab] OR Linoleic acids[tiab] OR Linoleic acid [tiab] OR Linolic acids[tiab] OR linolate[tiab] OR linoleate[tiab] OR Linolenate[tiab] OR "omega 3"[tiab] OR "omega 6"[tiab] OR omega3[tiab] OR omega6[tiab] OR (("n 3"[tiab] OR "n 6"[tiab]) AND (acid[tiab] OR acids[tiab])) OR "183 $\omega$ 3"[tiab] OR "18 3 $\omega$ 3"[tiab] OR "183omega3"[tiab] OR "18 3omega3"[tiab] OR $\omega$ 3[tiab] OR $\omega$ 6[tiab] Sort by: Most Recent	435,798
#3	Search: "Body Weight Changes" [Mesh] OR (("adipose tissue" [tiab] OR fat[tiab] OR weight[tiab]) AND (decreas* [tiab] OR chang* [tiab] OR loss [tiab] OR losing [tiab] OR reduc* [tiab])) OR "body weight" [tiab] OR "body weights" [tiab] Sort by: Most Recent	645,747
#1	Search: "Adiposity" [Mesh] OR "Adipose Tissue" [Mesh] OR "Adipocytes" [Mesh] OR adipocyte* [tiab] OR Adipose tissue* [tiab] OR Adipose body [tiab] OR Abdominal fat[tiab] OR Body fat[tiab] OR Fat cell[tiab] OR Fat cells[tiab] OR Fat pad[tiab] OR Fat pads[tiab] OR Fat tissue* [tiab] OR Fatty tissue* [tiab] OR Intraabdominal fat[tiab] OR Subcutaneous fat[tiab] OR Visceral fat[tiab] OR Intraabdominal fats[tiab] OR Subcutaneous fats[tiab] OR Visceral fats[tiab] Sort by: Most Recent	194,140



# E.2. Range of weight loss when consuming total diet replacements for weight control (Q2)

Date of search: 02 June 2020

#### Embase

Search	Query	Items identified
#10	#9 AND [english]/lim	3,547
#9	#7 NOT #8	3,685
#8	(rat:ti OR rats:ti OR mouse:ti OR mice:ti OR swine:ti OR porcine:ti OR murine:ti OR sheep:ti OR lambs:ti OR pigs:ti OR piglets:ti OR rabbit:ti OR rabbits:ti OR cat:ti OR cats:ti OR dog:ti OR dogs:ti OR cattle:ti OR bovine:ti OR monkey:ti OR monkeys:ti OR trout:ti OR marmoset*:ti) AND 'animal experiment'/de	1,062,853
#7	#5 NOT #6	3,690
#6	'animal experiment'/de NOT ('human experiment'/de OR 'human'/de)	2,247,064
#5	#3 AND #4	3,943
#4	'clinical trial'/exp OR 'randomization'/exp OR randomized:ti,ab OR randomised:ti,ab OR placebo:ti,ab OR randomly:ti,ab OR trial:ti,ab OR groups:ti,ab OR 'clinical trial (topic)'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'triple blind procedure'/exp OR (((singl* OR doubl* OR trebl* OR tripl*) NEAR/10 (mask* OR blind* OR dumm*)):ti,ab) OR 'crossover procedure'/exp OR (((crossoverOR 'cross over') NEAR/10 (study OR studies OR design* OR method* OR procedure OR comparison)):ti,ab) OR 'meta analysis'/exp OR 'meta analysis (topic)'/exp OR 'systematic review'/exp OR 'systematic review (topic)'/exp OR 'biomedical technology assessment//exp OR ((systematic* NEAR/3 (review* OR overview*)):ti,ab) OR ((methodologic* NEAR/3 (review* OR overview*)):ti,ab) OR ((methodologic* NEAR/3 (review* OR overview*)):ti,ab) OR ((collaborative NEAR/3 (review* OR overview*)):ti,ab) OR ((collaborative NEAR/3 (review* OR overview*)):ti,ab) OR ((collaborative NEAR/1 (synthes* OR extraction* OR abstraction*)):ti,ab) OR ((data NEAR/1 (synthes* OR extraction* OR abstraction*)):ti,ab) OR (arising':ti,ab OR 'hand search':ti,ab OR 'hand searching':ti,ab OR 'meta analysis':ti,ab OR metanaly*:ti,ab OR mediane:ti,ab OR cochrane:ti,ab OR 'meta analysis':ti,ab OR mediane:ti,ab OR cochrane:ti,ab OR 'meta regressions':ti,ab OR mediane:ti,ab OR 'meta regression*:ti,ab OR	5,425,604
#3	#1 AND #2	7,629
#2	'body weight loss'/exp OR (((weight OR fat OR 'adipose tissue') NEAR/3 (decreas* OR loss OR losing OR reduc*)):ti,ab,kw) OR ((weightNEAR/3 management):ti, ab,kw) OR ((chang* NEAR/3 ('adipose tissue' OR 'fat mass' OR 'fat tissue' OR weight)):ti, ab,kw)	332,351
#1	'low calorie diet'/exp/mj OR 'very low calorie diet'/exp/mj OR 'elimination diet'/exp/mj OR 'liquid diet'/exp/mj OR ((low NEAR/3 (calori* OR energy OR elimination) NEAR/5 (diet OR diets)):ti,ab,kw) OR vlcd:ti,ab,kw OR vled:ti,ab,kw OR lcd:ti,ab,kw OR (((ketogenic OR replacementOR 'meal substitute' OR liquid) NEAR/5 (diet OR diets)):ti, ab,kw) OR 'reducing diet':ti,ab,kw OR 'reducing diets':ti,ab,kw OR (((calori* OR energ*) NEAR/3 (reduc* OR restrict*) NEAR/5 (diet OR diets)):ti,ab,kw)	25,963



#### PubMed

Search	Query	Items identified
#14	Search: #12 AND #13 Sort by: Most Recent	2,806
#13	Search: ENGLISH[Language] Sort by: Most Recent	26,345,924
#12	Search: #11 Sort by: Most Recent	2,928
#11	Search: #10 and #7 Sort by: Most Recent	2,928
#10	Search: #8 OR #9 Sort by: Most Recent	3,717,566
#9	Search: Systematic[sb] OR meta-analysis[pt] OR meta-analysis as topic[Mesh] OR meta- analysis[Mesh] OR meta analy*[tw] OR metanaly*[tw] OR metaanaly*[tw] OR meta analy*[tw] OR integrative research[tiab] OR integrative review*[tiab] OR integrative overview*[tiab] OR research integration*[tiab] OR research overview*[tiab] OR collaborative review*[tiab] OR collaborative overview*[tiab] OR systematic review*[tiab] OR comparative efficacy[tiab] OR comparative effectiveness[tiab] OR outcomes research [tiab] OR indirect comparison*[tiab] OR Embase*[tiab] OR Cinahl*[tiab] OR systematic overview*[tiab] OR methodological overview*[tiab] OR methodologic overview*[tiab] OR methodological review*[tiab] OR methodologic review*[tiab] OR quantitative review* [tiab] OR quantitative overview*[tiab] OR quantitative synthes*[tiab] OR pooled analy* [tiab] OR cochrane[tiab] OR Medline[tiab] OR Pubmed[tiab] OR Medlars[tiab] OR handsearch*[tiab] OR hand search*[tiab] OR meta-regression*[tiab] OR metaregression* [tiab] OR data synthes*[tiab] OR data extraction[tiab] OR data abstraction*[tiab] OR mantel haenszel[tiab] OR peto[tiab] OR der-simonian[tiab] OR dersimonian[tiab] OR fixed effect*[tiab] OR "Cochrane Database Syst Rev"[Journal:jrid21711] Sort by: Most Recent	417,908
#8	Search: "clinical trial"[pt] OR "Random Allocation"[Mesh] OR randomized[tiab] OR randomised[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR "Clinical Trials as Topic"[Mesh] OR "Double-Blind Method"[Mesh] OR "Single-Blind Method"[Mesh] OR ((singl*[tiab] OR doubl*[tiab] OR trebl*[tiab] OR tripl*[tiab]) AND (mask*[tiab] OR blind*[tiab] OR dumm*[tiab])) OR "Cross-Over Studies"[Mesh] OR ((crossover[tiab] OR "cross over"[tiab]) AND (study[tiab] OR studies[tiab] OR design* [tiab] OR method*[tiab] OR procedure[tiab] OR comparison[tiab])) Sort by: Most Recent	3,456,468
#7	Search: #5 NOT #6 Sort by: Most Recent	5,493
#6	Search: (rat[ti] OR rats[ti] OR mouse[ti] OR mice[ti] OR swine[ti] OR porcine[ti] OR murine[ti] OR sheep[ti] OR lambs[ti] OR pigs[ti] OR piglets[ti] OR rabbit[ti] OR rabbits[ti] OR cat[ti] OR cats[ti] OR dog[ti] OR dogs[ti] OR cattle[ti] OR bovine[ti] OR monkey[ti] OR monkeys[ti] OR trout[ti] OR marmoset*[ti]) Sort by: Most Recent	2,006,904
#5	Search: #3 NOT #4 Sort by: Most Recent	5,732
#4	Search: ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) Sort by: Most Recent	4,704,526
#3	Search: ("Caloric Restriction"[Mesh] OR "Diet, Ketogenic"[Mesh] OR (("caloric reduction"[tiab] OR "calorie reduction"[tiab] OR "calories reduction"[tiab] OR "caloric restriction"[tiab] OR "calorie restriction"[tiab] OR "calories restriction"[tiab] OR "energy reduction"[tiab] OR "energy restriction"[tiab] OR "low caloric"[tiab] OR "low calorie"[tiab] OR "low calorie"[tiab] OR "low calorie"[tiab] OR "low calorie"[tiab] OR "total replacement"[tiab] OR "ketogenic diets"[tiab] OR "liquid diet"[tiab] OR "ketogenic diet"[tiab] OR "ketogenic diet"[tiab] OR "liquid diet"[tiab] OR "liquid diets"[tiab] OR "reducing diet"[tiab] OR "reducing diets"[tiab] OR "liquid diet"[tiab] OR "liquid diet"[tiab] OR "liquid diets"[tiab] OR "ketogent[tiab]) OR VLED[tiab] OR VLCD[tiab] OR ("adipose tissue"[tiab] OR fat[tiab] OR weight[tiab]) AND (decreas*[tiab] OR chang*[tiab] OR loss [tiab]	7,949
#2	Search: "Body Weight Changes" [Mesh:NoExp] OR "Weight Loss" [Mesh] OR (("adipose tissue" [tiab] OR fat[tiab] OR weight[tiab]) AND (decreas*[tiab] OR chang*[tiab] OR loss [tiab] OR losing[tiab] OR reduc*[tiab])) Sort by: Most Recent	553,343



Search	Query	Items identified
#1	Search: "Caloric Restriction"[Mesh] OR "Diet, Ketogenic"[Mesh] OR (("caloric reduction"[tiab] OR "calorie reduction"[tiab] OR "calories reduction"[tiab] OR "caloric restriction"[tiab] OR "calorie restriction"[tiab] OR "calories restriction"[tiab] OR "energy reduction"[tiab] OR "energy restriction"[tiab] OR "low caloric"[tiab] OR "low calorie"[tiab] OR "meal substitute"[tiab] OR "total replacement"[tiab] OR "ketogenic diet"[tiab] OR "ketogenic diets"[tiab] OR "liquid diets"[tiab] OR "liquid diets"[tiab] OR "reducing diet"[tiab] OR "reducing diets"[tiab] OR "liquid diets"[tiab] OR "low calories"[tiab] OR "liquid diets"[tiab] OR "ketogenic diet"[tiab] OR "ketogenic diets"[tiab] OR "liquid diets"[tiab] OR "liquid diets"[tiab] OR "ketogentent[tiab]) OR VLED[tiab] OR VLCD[tiab] OR LCD [tiab] Sort by: Most Recent	20,854

# E.3. Supplemental magnesium intake and risk of developing diarrhoea (Q3)

### Date of search: 22 June 2020

Embase

Search	Query	Items identified
#24	#14 AND #22 AND [english]/lim	5,340
#23	#14 AND #22	5,792
#22	#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21	5,441,679
#21	((data NEAR/1 (synthes* OR extraction* OR abstraction*)):ti,ab) OR handsearch*:ti,ab OR 'hand search':ti,ab OR 'hand searches':ti,ab OR 'hand searching':ti,ab OR 'mantel haenszel':ti,ab OR peto:ti,ab OR 'der simonian':ti,ab OR dersimonian:ti,ab OR 'fixed effect':ti,ab OR 'fixed effects':ti,ab OR 'latin square':ti,ab OR 'latin squares':ti,ab OR 'meta analysis':ti,ab OR 'meta analyses':ti,ab OR 'met analysis':ti,ab OR 'meta analyses':ti,ab OR metaanaly*:ti,ab OR metaanaly*:ti,ab OR 'meta analyses':ti,ab OR 'meta effects':ti,ab OR 'meta analysis':ti,ab OR 'meta regressions':ti,ab OR metaregression*:ti,ab OR medline:ti,ab OR cochrane:ti,ab OR pubmed:ti,ab OR medlars:ti,ab OR embase:ti,ab OR cinahl:ti,ab OR cochrane:jt OR 'evidence report':jt OR ((comparative NEAR/3 (efficacy OR effectiveness)):ti,ab) OR 'outcomes research':ti,ab OR 'relative effectiveness':ti,ab OR (((indirect OR 'indirect treatment' OR 'mixed treatment') NEAR/3 comparison):ti,ab)	457,245
#20	((systematic* NEAR/3 (review* OR overview*)):ti,ab) OR ((methodologic* NEAR/3 (review* OR overview*)):ti,ab) OR ((quantitative NEAR/3 (review* OR overview* OR synthes*)):ti,ab) OR ((research NEAR/3 (integrati* OR overview*)):ti,ab) OR ((integrative NEAR/3 (review* OR overview*)):ti,ab) OR ((collaborative NEAR/3 (review* OR overview*)):ti,ab) OR ((pool* NEAR/3 analy*):ti, ab)	273,287
#19	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR 'systematic review'/exp OR 'systematic review (topic)'/exp OR 'biomedical technology assessment'/exp	402,087
#18	<pre>`crossover procedure'/exp OR (((crossover OR 'cross over') NEAR/10 (study OR studies OR design* OR method* OR procedure OR comparison)):ti,ab)</pre>	93,442
#17	((singl* OR doubl* OR trebl* OR tripl*) NEAR/10 (mask* OR blind* OR dumm*)):ti,ab	249,335
#16	'clinical trial (topic)'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'triple blind procedure'/exp	532,591
#15	'clinical trial'/exp OR 'randomization'/exp OR randomized:ti,ab OR randomised:ti,ab OR placebo:ti,ab OR randomly:ti,ab OR trial:ti,ab OR groups:ti,ab OR (group1:ti,ab AND group 2:ti,ab)	4,864,364
#14	#12 NOT #13	16,546
#13	(rat:ti OR rats:ti OR mouse:ti OR mice:ti OR swine:ti OR porcine:ti OR murine:ti OR sheep:ti OR lambs:ti OR pigs:ti OR piglets:ti OR rabbit:ti OR rabbits:ti OR cat:ti OR cats:ti OR dog:ti OR dog:ti OR cattle:ti OR bovine:ti OR monkey:ti OR monkey:ti OR trout:ti OR marmoset*:ti) AND 'animal experiment'/de	1,064,998
#12	#10 NOT #11	16,569



Search	Query	Items identified
#11	'animal experiment'/de NOT ('human experiment'/de OR 'human'/de)	2,250,526
#10	#3 OR #6 OR #8 OR #9	18,100
#9	('magnesium'/exp OR 'magnesium salt'/exp OR magnesium:ti,ab,kw) AND ('dietary supplement'/exp OR 'fortified food'/exp OR 'diet'/de) OR ((magnesium NEAR/3 (intak* OR supplement* OR therap* OR diet*;ti,ab,kw)):ti,ab,kw) OR 'mg supplement*': ti,ab,kw OR 'mg fortified':ti,ab,kw OR 'magnesium intake'/exp OR 'magnesium'/mj/dd_dt OR 'magnesium salt'/mj/dd_dt	9,906
#8	#6 OR #7	6,767
#7	`magnesium'/exp/dd_ae,dd_to OR 'magnesium salt'/exp/dd_ae,dd_to	1,092
#6	#4 AND #5	5,886
#5	'adverse event'/de OR 'adverse drug reaction'/exp OR 'intoxication'/de OR 'drug intoxication'/exp OR 'drug overdose'/exp OR 'toxicity'/exp OR 'contraindication'/exp OR 'risk'/de OR 'risk factor'/exp OR 'risk assessment'/exp OR 'safety'/de OR 'patient safety'/exp OR 'food safety'/exp OR 'drug safety'/exp OR adverse:ti,ab,kw OR (((undesirable OR harm* OR serious OR negative OR side OR unwanted OR untoward) NEAR/5 (effect* OR reaction* OR event* OR interaction* OR outcome* OR response* OR sequala* OR sequela*)):ti,ab, kw) OR intoxic*:ti,ab,kw OR toxic*:ti,ab,kw OR overdose*:ti,ab,kw OR ((risk* NEAR/5 (assessment* OR factor*)):ti,ab,kw) OR contraindication*:ti,ab,kw OR 'contra indication': ti,ab,kw OR 'contra indications':ti,ab,kw OR safe:ti,ab,kw OR safety:ti,ab,kw	5,724,197
#4	`magnesium'/exp/mj OR 'magnesium salt'/exp/mj OR 'magnesium intake'/exp/mj OR magnesium:ti	44,385
#3	#1 AND #2	4,041
#2	'tolerability'/exp OR 'diarrhea'/exp OR diarrhe*:ti,ab,kw OR diarrhoe*:ti,ab,kw OR dysenter*:ti,ab,kw OR 'feces'/exp OR feces:ti,ab,kw OR faec*:ti,ab,kw OR fecal:ti,ab, kw OR laxative:ti,ab,kw OR stool:ti,ab,kw OR stools:ti,ab,kw OR tolerab*:ti,ab,kw OR ((osmotic NEAR/3 (effect OR effects)):ti,ab,kw)	636,059
#1	'magnesium'/exp OR 'magnesium intake'/exp OR 'magnesium salt'/exp OR magnesium:ti, ab,kw	127,141

### PubMed

Search	Query	Items identified
#19	Search: "english"[Language] AND #18 Sort by: Most Recent	4,751
#18	Search: #17 AND #14 Sort by: Most Recent	5,231
#17	Search: #16 OR #15 Sort by: Most Recent	3,731,983
#16	Search: systematic[sb] OR meta-analysis[pt] OR meta-analysis as topic[Mesh] OR meta- analysis[Mesh] OR meta analy*[tw] OR metanaly*[tw] OR metaanaly*[tw] OR meta analy*[tw] OR integrative research[tiab] OR integrative review*[tiab] OR integrative overview*[tiab] OR research integration*[tiab] OR research overview*[tiab] OR collaborative review*[tiab] OR collaborative overview*[tiab] OR systematic review*[tiab] OR comparative efficacy[tiab] OR comparative effectiveness[tiab] OR outcomes research [tiab] OR indirect comparison*[tiab] OR Embase*[tiab] OR Cinahl*[tiab] OR systematic overview*[tiab] OR methodological overview*[tiab] OR methodologic overview*[tiab] OR methodological review*[tiab] OR methodologic review*[tiab] OR quantitative review* [tiab] OR quantitative overview*[tiab] OR quantitative synthes*[tiab] OR pooled analy* [tiab] OR cochrane[tiab] OR Medline[tiab] OR Pubmed[tiab] OR Medlars[tiab] OR handsearch*[tiab] OR hand search*[tiab] OR meta-regression*[tiab] OR metaregression* [tiab] OR data synthes*[tiab] OR data extraction[tiab] OR data abstraction*[tiab] OR mantel haenszel[tiab] OR peto[tiab] OR der-simonian[tiab] OR dersimonian[tiab] OR fixed effect*[tiab] OR "Cochrane Database Syst Rev"[Journal:jrid21711] Sort by: Most Recent	421,144



Search	Query	Items identified
#15	Search: "clinical trial"[pt] OR "Random Allocation"[Mesh] OR randomized[tiab] OR randomised[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR (group 1[tiab] AND group 2[tiab]) OR "Clinical Trials as Topic"[Mesh] OR "Double-Blind Method"[Mesh] OR "Single-Blind Method"[Mesh] OR ((singl*[tiab] OR doubl*[tiab] OR trebl*[tiab] OR tripl*[tiab]) AND (mask*[tiab] OR blind*[tiab] OR dumm*[tiab])) OR "Cross-Over Studies"[Mesh] OR ((crossover[tiab] OR "cross over"[tiab]) AND (study[tiab] OR studies[tiab] OR design*[tiab] OR method*[tiab] OR procedure[tiab] OR comparison [tiab])) Sort by: Most Recent	3,468,659
#14	Search: #12 NOT #13 Sort by: Most Recent	16,416
#13	Search: (rat[ti] OR rats[ti] OR mouse[ti] OR mice[ti] OR swine[ti] OR porcine[ti] OR murine[ti] OR sheep[ti] OR lambs[ti] OR pigs[ti] OR piglets[ti] OR rabbit[ti] OR rabbits[ti] OR cat[ti] OR cats[ti] OR dog[ti] OR dogs[ti] OR cattle[ti] OR bovine[ti] OR monkey[ti] OR monkeys[ti] OR trout[ti] OR marmoset*[ti]) Sort by: Most Recent	2,009,802
#12	Search: #10 NOT #11 Sort by: Most Recent	16,693
#11	Search: ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) Sort by: Most Recent	4,709,914
#10	Search: #3 OR #8 OR #9 Sort by: Most Recent	21,965
#9	Search: (("Magnesium"[Mesh] OR Magnesium[tiab]) AND ("Dietary Supplements"[Mesh:noexp] OR "Food, Fortified"[Mesh] OR "Diet"[Mesh:NoExp] OR diet* [tiab] OR intak*[tiab] OR supplement*[tiab] OR therap*[tiab])) OR "Mg supplement*"[tiab] OR "Mg fortified"[tiab] OR "Magnesium/therapeutic use"[Mesh] Sort by: Most Recent	19,040
#8	Search: (("Magnesium"[Majr] OR magnesium[ti]) AND ("Drug-Related Side Effects and Adverse Reactions"[Mesh] OR "Poisoning"[Mesh] OR "Drug Hypersensitivity"[Mesh] OR "Drug Overdose"[Mesh] OR "Contraindications"[Mesh] OR "Risk"[Mesh] OR "Risk Factors"[Mesh] OR "Risk Assessment"[Mesh:NoExp] OR "Safety"[Mesh:NoExp] OR "Patient Safety"[Mesh] OR "Food Safety"[Mesh] OR adverse[tiab] OR contraindication* [tiab] OR "contra indication*"[tiab] OR safe[tiab] OR safety[tiab] OR risk assessment* [tiab] OR "sk factor*[tiab] OR ((undesirable[tiab] OR harm*[tiab] OR serious[tiab] OR negative[tiab] OR side[tiab] OR unwanted[tiab] OR untoward[tiab]) AND (effect*[tiab] OR reaction*[tiab] OR sequela*[tiab] OR sequela*[tiab])))) OR ("magnesium/adverse effects"[MeSH Terms] OR "magnesium/poisoning"[MeSH Terms] OR "magnesium/ toxicity"[MeSH Terms]) Sort by: Most Recent	3,954
#7	Search: "magnesium/adverse effects"[MeSH Terms] OR "magnesium/poisoning"[MeSH Terms] OR "magnesium/toxicity"[MeSH Terms] Sort by: Most Recent	580
#6	Search: ("Magnesium"[Majr] OR magnesium[ti]) AND ("Drug-Related Side Effects and Adverse Reactions"[Mesh] OR "Poisoning"[Mesh] OR "Drug Hypersensitivity"[Mesh] OR "Drug Overdose"[Mesh] OR "Contraindications"[Mesh] OR "Risk"[Mesh] OR "Risk Factors"[Mesh] OR "Risk Assessment"[Mesh:NoExp] OR "Safety"[Mesh:NoExp] OR "Patient Safety"[Mesh] OR "Food Safety"[Mesh] OR adverse[tiab] OR contraindication* [tiab] OR "contra indication*"[tiab] OR safe[tiab] OR safety[tiab] OR risk assessment* [tiab] OR risk factor*[tiab] OR ((undesirable[tiab] OR harm*[tiab] OR serious[tiab] OR negative[tiab] OR side[tiab] OR unwanted[tiab] OR untoward[tiab]) AND (effect*[tiab] OR reaction*[tiab] OR sequala*[tiab] OR sequela*[tiab]))) Sort by: Most Recent	3,497
#5	Search: "Drug-Related Side Effects and Adverse Reactions"[Mesh] OR "Poisoning"[Mesh] OR "Drug Hypersensitivity"[Mesh] OR "Drug Overdose"[Mesh] OR "Contraindications"[Mesh] OR "Risk"[Mesh] OR "Risk Factors"[Mesh] OR "Risk Assessment"[Mesh:NoExp] OR "Safety"[Mesh:NoExp] OR "Patient Safety"[Mesh] OR "Food Safety"[Mesh] OR adverse[tiab] OR contraindication*[tiab] OR "contra indication*"[tiab] OR safe[tiab] OR safety[tiab] OR risk assessment*[tiab] OR risk factor* [tiab] OR ((undesirable[tiab] OR harm*[tiab] OR serious[tiab] OR negative[tiab] OR side [tiab] OR unwanted[tiab] OR untoward[tiab]) AND (effect*[tiab] OR reaction*[tiab] OR event*[tiab] OR interaction*[tiab] OR outcome*[tiab] OR response*[tiab] OR sequala* [tiab] OR sequela*[tiab])) Sort by: Most Recent	3,758,191

Search	Query	Items identified
#4	Search: "Magnesium"[Majr] OR magnesium[ti] Sort by: Most Recent	34,053
#3	Search: ("Magnesium"[Mesh] OR magnesium[tiab]) AND ("Diarrhea"[Mesh] OR diarrhe* [tiab] OR diarrho*[tiab] OR dysenter*[tiab]OR "Feces"[Mesh] OR feces[tiab] OR fecal [tiab] OR faec*[tiab] OR laxative[tiab] OR stool*[tiab] OR osmotic effect*[tiab] OR tolerab*[tiab]) Sort by: Most Recent	1,978
#2	Search: "Diarrhea" [Mesh] OR diarrhe* [tiab] OR diarrho* [tiab] OR dysenter* [tiab] OR "Feces" [Mesh] OR feces [tiab] OR fecal [tiab] OR faec* [tiab] OR laxative [tiab] OR stool* [tiab] OR osmotic effect* [tiab] OR tolerab* [tiab] Sort by: Most Recent	370,900
#1	Search: "Magnesium"[Mesh] OR magnesium[tiab] Sort by: Most Recent	101,094

# E.4. Fat content of energy-restricted diets and risk of gallstone formation (Q4)

### Date for search: 9 December 2020

#### Embase

Search	Query	Items identified
#9	#8 AND [2013-2021]/py	67
#8	#7 AND [english]/lim	160
#7	#5 NOT #6	179
#6	(rat:ti OR rats:ti OR mouse:ti OR mice:ti OR swine:ti OR porcine:ti OR murine:ti OR sheep:ti OR lambs:ti OR pigs:ti OR piglets:ti OR rabbit:ti OR rabbits:ti OR cat:ti OR cats:ti OR dog:ti OR dogs:ti OR cattle:ti OR bovine:ti OR monkey:ti OR monkeys:ti OR trout:ti OR marmoset*:ti) AND 'animal experiment'/de	1,089,880
#5	#3 NOT #4	178
#4	`animal experiment'/de NOT (`human experiment'/de OR 'human'/de)	2,294,858
#3	#1 AND #2	183
#2	'biliary sludge'/exp OR 'cholelithiasis'/exp OR 'gallbladder'/exp OR 'gallbladder function'/ exp OR (((bile OR biliary) NEAR/3 (calculus OR calculi OR sludge*)):ti,ab,kw) OR cholelith*:ti,ab,kw OR cholecystolithias*:ti,ab,kw OR gallbladder*:ti,ab,kw OR 'gall bladder*':ti,ab,kw OR gallsludge*:ti,ab,kw OR 'gall sludge*':ti,ab,kw OR gallstone*:ti,ab, kw OR 'gall stone*':ti,ab,kw OR 'vesica biliaris':ti,ab,kw OR 'vesica fellea':ti,ab,kw	121,762
#1	'low calorie diet'/exp/mj OR 'very low calorie diet'/exp/mj OR 'elimination diet'/exp/mj OR 'liquid diet'/exp/mj OR ((low NEAR/3 (calori* OR energy OR elimination) NEAR/5 (diet OR diets)):ti,ab,kw) OR vlcd:ti,ab,kw OR vled:ti,ab,kw OR lcd:ti,ab,kw OR (((ketogenic OR replacement OR 'meal substitute' OR liquid) NEAR/5 (diet OR diets)):ti,ab,kw) OR 'reducing diet':ti,ab,kw OR 'reducing diets':ti,ab,kw OR (((calori* OR energ*) NEAR/3 (reduc* OR restrict*) NEAR/5 (diet OR diets)):ti,ab,kw)	26,839

### Pubmed

Search	Query	Items identified
#9	(#8) AND (("2014"[Date - Publication]: "3000"[Date - Publication]))	14
#8	#7 AND ENGLISH[Language]	56
#7	#5 NOT #6	69
#6	(rat[ti] OR rats[ti] OR mouse[ti] OR mice[ti] OR swine[ti] OR porcine[ti] OR murine[ti] OR sheep[ti] OR lambs[ti] OR pigs[ti] OR piglets[ti] OR rabbit[ti] OR rabbits[ti] OR cat[ti] OR cats[ti] OR dog[ti] OR dogs[ti] OR cattle[ti] OR bovine[ti] OR monkey[ti] OR monkeys[ti] OR trout[ti] OR marmoset*[ti])	2,307,004
#5	#3 NOT #4	69
#4	("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))	4,762,683



Search	Query	Items identified
#3	#1 AND #2	80
#2	"Cholecystolithiasis"[Mesh] OR "Gallbladder"[Mesh] OR "Gallbladder Emptying"[Mesh] OR "Gallstones"[Mesh] OR "bile duct calcul*"[tiab] OR "bile duct sludge*"[tiab] OR "bile calcul*"[tiab] OR "bile sludge*"[tiab] OR "biliary calcul*"[tiab] OR "biliary sludge"[tiab] OR "biliary system calcul*"[tiab] OR "biliary system sludge*"[tiab] OR cholelith*[tiab] OR cholecystolithias*[tiab] OR gallbladder*[tiab] OR "gall bladder*"[tiab] OR gallsludge[tiab] OR "gall sludge*"[tiab] OR gallstone*[tiab] OR "gall stone*"[tiab] OR "vesica biliaris"[tiab] OR "vesica fellea"[tiab]	68,834
#1	"Caloric Restriction"[Mesh] OR "Diet, Ketogenic"[Mesh] OR (("caloric reduction"[tiab] OR "calorie reduction"[tiab] OR "calories reduction"[tiab] OR "caloric restriction"[tiab] OR "calorie restriction"[tiab] OR "calories restriction"[tiab] OR "energy reduction"[tiab] OR "energy restriction"[tiab] OR "low caloric"[tiab] OR "low calorie"[tiab] OR "low calories"[tiab] OR "low energy"[tiab] OR "meal replacement"[tiab] OR meal substitute"[tiab] OR "total replacement"[tiab] OR "ketogenic diets"[tiab] OR "liquid diet"[tiab] OR "liquid diets"[tiab] OR "reducing diet"[tiab] OR "reducing diets"[tiab] OR ("total diet"[tiab] AND replacement[tiab]) OR VLED[tiab] OR VLCD[tiab] OR LCD[tiab]	21,663