## Appendix G - Forest plots. Intervention studies on metabolic diseases

Figure G.1: Randomised controlled trials: effect of high vs. low sugar intake on measures of body fatness.


Figure G.1a: Effect of high vs low sugar intake on body weight (kg)


Figure G.1b: Effect of high vs low sugar intake on BMI (kg/m2)


Figure G.1c: Effect of high vs low sugar intake on waist circumference (cm)


Footnote to Figure G1. * differences in BW change between high and low sugar intake, $\mathrm{AL}=$ add libitum; $\mathrm{BMI}=$ body mass index; $\mathrm{BW}=$ body weight; $\mathrm{CI}=$ confidence interval; $\mathrm{E} \%=$ energy percentage; $\mathrm{Eu}=\mathrm{eucaloric;} \mathrm{~F}=$ females; GP = general population; H-TG = hyper-triglyceridemic; MF = males and females; Mix under Sugar = sugar mixtures; Mixed under Source = foods and beverages; N=average sample size per arm; OB = obese; OW = overweight; RoB = risk of bias (tier); $\mathrm{r05}$ and r099 $=$ change in the significance of the effect ( $0=$ no change; $1=$ change) when assuming a correlation coefficient of respectively 0.50 and 0.99 (instead of 0.82 ) when computing the SE of the effect measurement. Study duration is expressed in weeks.

Figure G.1d: Effect of high vs low sugar intake on body fat (\%)

Figure G.2: Randomised controlled trials: effect of high vs. low sugar intake on measures of ectopic fat deposition


Figure G.2a: Effect of high vs low sugar intake on liver fat (standardized mean difference)

( and females; Mix under Sugar = sugar mixtures; Mix under Source = foods and beverages; $N=$ average sample size per arm; NAFLD = non-alcoholic fatty liver disease; $\mathrm{OB}=\mathrm{obese}$; $\mathrm{OW}=\mathrm{overweight;} \mathrm{RoB}=$ risk of bias (tier); r05 and r099 = change in the significance of the effect ( $0=$ no change; $1=$ change) when assuming a correlation coefficient of respectively 0.50 and 0.99 (instead of 0.82 ) when computing the SE of the effect measurement; SMD = standardized mean difference. Study duration is expressed in weeks.

Figure G.2b: Effect of high vs low sugar intake on visceral adipose tissue (standardized mean difference)

Figure G.3: Randomised controlled trials: effect of fructose vs. glucose on measures of ectopic fat deposition


Figure G.3a: Effect of fructose vs glucose on liver fat (standardized mean difference)

| Study | N | SMD Effect | se Effect | 95\% cl | r 0.5 | r 0.99 |  |  |  | Fru-Glu (E\%) | Sex | Subjects | Source | BW* | Weeks | RoB |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Diet = Isocaloric with positive energy balance |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Silbernagel et al, 2011 | 9 | 0.00 | 0.15 | [-0.30; 0.30] | 0 | 0 |  |  |  | 22 | MF | BMİ35 | в | -1.5 | 4 | 1 |
| Random effects model |  | 0.00 |  | [-0.30; 0.30] |  |  |  |  |  |  |  |  |  |  |  |  |
| Hetergeneity: not applicat |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Diet $=$ Ad libitum |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Stanhope et al, 2009* | 15 | 0.54 | 0.09 | [ $0.36 ; 0.72$ ] | 0 | 0 |  |  | - | 25 | MF | ош/ов | в | -0.2 | 8 | 2 |
| Random effects model |  | 0.54 |  | [0.36; 0.72] |  |  |  |  |  |  |  |  |  |  |  |  |
| Heterogeneity: not applicat |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Random effects model |  | 0.28 |  | [-0.25; 0.82] |  |  |  |  |  |  |  |  |  |  |  |  |
| Heterogeneity: $I^{2}=50 \%[81 \% ; 97 \%], \tau^{2}=0.1320, p<0.01$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $I^{2}=\mathrm{NA} \%, p=\mathrm{NA}$   <br> Random effects model $(r=0.5): 0.28[-3.16 ; 3.73]$ $-1 \quad-0.5 \quad 0$ 0.5 <br> Relack $=$ Parallel Red $=$ Cro  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

Footnote to Figure G3. * differences in BW change between high and low sugar intake; $\mathrm{AO}=$ abdominal obesity; $\mathrm{B}=$ beverages; $\mathrm{BMI}=$ body mass index; $\mathrm{BW}=$ body weight; $\mathrm{Cl}=$ confidence interval; $\mathrm{E} \%=$ energy percentage;
 effect ( $0=$ no change; $1=$ change) when assuming a correlation coefficient of respectively 0.50 and 0.99 (instead of 0.82 ) when computing the SE of the effect measurement; RoB $=$ risk of bias (tier); SMD $=$ standardized mean difference. Study duration is expressed in weeks.

Figure G.3b: Effect of fructose vs glucose on visceral adipose tissue (standardized mean difference)

Figure G.4: Randomised controlled trials: effect of high vs. low sugar intake on measures of glucose tolerance


Figure G.4a: Effect of high vs low sugar intake on blood glucose at $120^{\prime}$ during an OGTT ( $\mathrm{mg} / \mathrm{dL}$ )


Figure G.4b: Effect of high vs low sugar intake on insulin at $120^{\prime}$ during an OGTT (pmol/L)

Figure G.4c: Effect of high vs low sugar intake on fasting glucose ( $\mathrm{mg} / \mathrm{dL}$ )


Figure G.4c1: Stratified by type of diet


Figure G.4c2: Stratified by sugars source

| Study | N | Mean Effect | se Effect | 95\% Cl | r 0.5 | r0.99 |  |  |  | Sugar diff (E\%) | Sex | Subjects | Sugar | Source | Bw- | Duration | RoB |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Diet = Isocaloric with neutral energy balance |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lewis et al, 2013 | 13 | 20.02 | 1.52 | [23.05; 29.00] | 0 | 0 | + |  |  | 10 | MF | owor | Mix | Mix | 0.7 | 0 | 1 |
| Blacketal. 2000 | 13 | 6.94 | 5.43 | [-3.70; 17.58] | 0 | 2 |  |  |  | 15 | m | 8M\|×35 | Mix | Mix | 0.4 | $\bigcirc$ | 1 |
| Halltisch ef al, 19833* (normoinsulinemic) | 12 | -2.36 | 3.33 | [-8.89; 4.17] | 0 | 2 |  |  |  | 15 | m | $\mathrm{N}-1$ | Fruct | F |  | 5 | 2 |
| Helltrisch et al, 19830* (hyperinsulinemic) | 12 | 17.03 | 3.29 | [11.18; 24.08] | 0 | 0 | \# |  |  | 15 | m | H-1 | Fiuct | F |  | 5 | 2 |
| Lowndes et al, 2015 | 32 | 7.70 | 4.98 | [-2.07; 17.47] | 0 | 2 | H |  |  | 18 | MF | вм1<35 | Mix | B |  | 10 | 1 |
| Umpleby et al, 2017 (No NaFLD) | 14 | 1.39 | 8.18 | [-14.85; 17.42] | 0 | 0 |  |  |  | 20 | m | owno-Naflo | Mix | Mix | 22 | 12 | 2 |
| Umpleby et al, 2017 (NAFLD) | 11 | -1.39 | 8.20 | [-17.48; 14.89] | 0 | 0 |  |  |  | 20 | m | ownaflo | Mix | Mix | 2.1 | 12 | 2 |
| lsasel et al, 1983* | 12 | 113.82 | 18.31 | [77.93; 149.70] | 0 | 0 |  | \# |  | 28 | M | H-1 | Mix | F | -3.8 | 6 | 1 |
| lysel et al. 1983* | 12 | 71.48 | 10.07 | [51.74: 91.22] | 0 | 0 |  | 푼 |  | 28 | F | H-1 | Mix | F | 0.2 | 8 | 1 |
| Moseret st, 1988 (OC-Usens) | 6 | 0.00 | 6.58 | [-12.90; 12.90] | 0 | 0 |  |  |  | 43 | F | oc | Mix | F | -1 | 4 | 1 |
| Moseret al. 1988 ( No 0 OC -users) | 6 | 0.00 | 12.49 | [-24.48: 24.48] | 0 | 0 |  |  |  | 43 | F | Non-OC | Mix | F | 1 | 4 | 1 |
| Random effects model $(r=0.82) \quad 19.99 \quad[0.67 ; 39.31]$Hetergenety: $I^{1}=93 \%[90 \%: 98 \%), z^{2}=998.7957, p<0.01$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Diet $=$ Ad libilum |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Maney et al. 2010 | 48 | 2.40 | 1.77 | [-1.07: 5.87$]$ | 0 | 2 | - |  |  | 10 | MF | Non-Ob | Mix | Mix | 0.1 | 8 | 1 |
| Campos et al 2015 | ${ }^{13}$ | 15.27 | 12.63 | [-9.48; 40.02] | 0 | 2 | I- |  |  | 18 | MF | ow/ob | Mix | B | 2.3 | 12 | 1 |
| Maersk et al, $2012^{*}$ | 14 | 6.40 | 7.11 | [-7.53; 20.33] | 0 | 2 |  |  |  | 18 | MF | Ow/OB | Mix | B | 1 | 24 | 2 |
| Saris et al, 2000* | 79 | 15.13 | 8.25 | [-1.05; ${ }^{\text {12,31] }}$ | 0 | 0 | $\square$ |  |  | 19 | MF | ow/ob | Mix | Mix | 0.9 | 24 | 1 |
| Raben et al, 2002* | 11 | 13.00 | 5.70 | [ 1.83; 24.17] | 1 | 0 | $\square$ |  |  | 23 | MF | ow | Mix | Mix | 2.0 | 10 | 1 |
| Random effects model ( $r=0.82$ ) |  | 7.58 |  | [ 1.04; 14.12] |  |  | - |  |  |  |  |  |  |  |  |  |  |
| Hewergenety : $i^{2}=38 \% 105 \%$ >75\%1, $\tau^{2}=21.4500, p=0.20$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Random effects model ( $\mathrm{r}=0.82$ ) |  | 16.21 |  | [ 3.91; 28.50] |  |  | - |  |  |  |  |  |  |  |  |  |  |
| Prediction interval [-36.56; 68.97] |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Heterogentiy: $t^{2}=93 \%$ [ $900 \%$ : 95\%], $\tau^{2}=565.7927, p<0.01$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Residual heterogeneity: $t^{2}=91 \%[37 \% ; 94 \%]$ ] $p<0.01$ <br> Random effects model ( $r=0.5$ ): 12.85 [1.89; 23.81] |  |  |  |  |  |  | 50 | $50 \quad 100$ |  |  |  |  |  |  |  |  |  |
| Random effects mosel ( $r=0.99$ ) 18.04 (1.65; |  |  |  | 1 $\rightarrow$ significant |  |  |  | $0.99=2 \rightarrow$ no | signifion | effect (0.82) | mes | ificant (0.99) |  |  |  |  |  |

Footnote to Figure G4. * differences in BW change between high and low sugar intake; B = beverages; BMI = body mass index; $\mathrm{BW}=$ body weight; CI $=$ confidence interval; E\% = energy percentage; F under Sex = females; F under Source = food; Fruct = fructose; GP = general population; H-I = hyperinsulinemia; M = males; MF = males and females; Mix under Sugar = sugar mixtures; Mix under Source = foods and beverages; $\mathrm{N}=$ average sample size per arm; $\mathrm{N}-\mathrm{I}=$ normo-insulinemia; NAFLD = non-alcoholic fatty liver disease; OB = obese; OC = oral contraceptives; OW = overweight; r05 and r099 = change in the significance of the effect ( $0=$ no change; $1=$ change) when assuming a correlation coefficient of respectively 0.50 and 0.99 (instead of 0.82 ) when computing the SE of the effect measurement; RoB = risk of bias (tier). Study duration is expressed in weeks.

Figure G.4d: Effect of high vs low sugar intake on fasting insulin (pmol/L)

Figure G.5: Randomised controlled trials: effect of fructose vs. glucose on measures of glucose tolerance


Figure G.5a: Effect of fructose vs glucose on fasting glucose ( $\mathrm{mg} / \mathrm{dL}$ )

| Study | N | Mean Effect | se Effect | 95\% Cl | ${ }^{0} 0.5$ | r 0.9 |  |  |  |  | Fru-Glu (E\%) | Sex | Subjects | Source | BW* | Weeks | Rob |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Diet = Isocaloric with neutral energy balance |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lowndes et al. 2015 | 32 | 22.30 | 10.38 | [ 1.95; 42.85] | 1 | 0 |  | $\square$ |  |  | 9.00 | MF | вM1<35 | E |  | 10 | 1 |
| Koh et al, 1988 (NGT) | 9 | -80.04 | 18.18 | [-91.78; -28.33] | 0 | 0 | $\square$ |  |  |  | 15.00 | MF | NGT | Mix |  | 4 | 2 |
| Koh et al, 1988 (IGT) | 9 | -20.01 | 28.38 | [-71.72; 31.69] | 0 | 2 |  |  |  |  | 15.00 | MF | 1 IGT | Mix |  | 4 | 2 |
| Kelsay et sl, 1974 | 7 | 0.00 | 10.62 | [-20.81; 20.81] | 0 | 0 |  |  |  |  | 42.50 | F | GP | F |  | 4 | 2 |
| Random effects model |  | -12.48 |  | [48.46; 23.50] |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Heterogeneity: $t^{2}=34 \%$ [80 | 294\% | $=1089.3313 . \mathrm{p}$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Diet = Isocaloric with positive energy balance |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Silbernagel et al, 2011 | 10 | $-5.00$ | 11.40 | [-27.35; 17.35] | 0 | 0 |  |  |  |  | 22.00 | MF | BM1<35 | E | $-1.5$ | 4 | 1 |
| Random effects model Heterogeneity: not applica |  | -5.00 |  | [-27.35; 17.35] |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Diet $=$ Ad libitum |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mark et al, 2014 | 35 | 7.38 | 5.73 | [-3.86; 18.62] | 0 | 2 |  |  |  |  | 16.00 | F | ow/ob | E | -0.4 | 4 | 1 |
| Jin et al. 2014 | 10 | 149.21 | 61.65 | [28.38: 270.04] | 1 | 0 |  |  |  |  | 20.00 | MF | NAFLD | B | 0.2 | 4 | 1 |
| Stanhope et al. $2009^{*}$ | 16 | 6.25 | 11.70 | [-16.68: 29.17] | , | - |  | + |  |  | 25.00 | MF | OW/OB | - | -0.2 | 8 | 2 |
| Random effects model |  | 8.14 |  | [-1.91; 18.20] |  |  |  | - |  |  |  |  |  |  |  |  |  |
| Heterogeneity: $t^{2}=62 \%[0 \% ;>89 \%], z^{2}=<0.0001, p=0.07$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Random effects model |  | -0.77 |  | [-20.07; 18.53] |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Prediction interval $r^{\text {a }}$, |  |  |  | [-61.75; 60.20] |  |  |  |  |  |  |  |  |  |  |  |  |  |
| $\text { Residual heterogeneity: } I^{2}=79 \%[55 \% ; 91 \%], p<0.01$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  | ${ }^{-100}$ = Parallel | $\text { Red }=\text { Cros }$ | 200 | 300 |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

Footnote to Figure G5. * differences in BW change between high and low sugar intake; $B=$ beverages; $B M I=$ body mass index; $B W=$ body weight; $C I=$ confidence interval; $\mathrm{E} \%=$ energy percentage; $F$ under Sex $=$ females; $F$ under Source = food; Fru = fructose; Glu = glucose; GP = general practitioner; $\operatorname{IGT}=$ impaired glucose tolerance; MF = males and females; Mix = foods and beverages; $N=$ average sample size per arm; NAFLD = non-alcoholic fatty liver disease; $\mathrm{NGT}=$ normal glucose concentration; $\mathrm{OB}=$ obese; $\mathrm{OW}=$ overweight; r 05 and r099 = change in the significance of the effect ( $0=$ no change; $1=$ change) when assuming a correlation coefficient of respectively 0.50 and 0.99 (instead of 0.82 ) when computing the SE of the effect measurement; RoB $=$ risk of bias (tier). Study duration is expressed in weeks.

Figure G.5b: Effect of fructose vs glucose on fasting insulin (pmol/L)

Figure G.6: Randomised controlled trials: effect of high vs. low sugar intake on blood lipids
Figure G.6a: Effect of high vs low sugar intake on total cholesterol ( $\mathrm{mg} / \mathrm{dL}$ )


Figure G.6a1: Stratified by type of diet

| Study | N | Mean Effect | se Effect | $95 \% \mathrm{Cl}$ | ${ }^{0} 0.5$ | r 0.99 |  |  | Sugar diff (E\%) | Sex | Subject | Sugar | Diet | BW* | Weeks | RoB |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Source $=$ Beverages |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Majid et sl, 2013 | 31 | -28.88 | 4.44 | [-35.39; -17.98] | 0 | 0 | $\mp$ |  | 8.00 | M | GP | Mix | AL |  | 4 | 2 |
| Lowndes et al. 2014a | 15 | -14.30 | 8.14 | [-30.28: 1.88 ] | 0 | 2 |  |  | 10.00 | MF | оw/ob | Mix | Eu | 0 | 10 | 2 |
| Campos et sl, 2015 | 13 | 0.00 | 8.88 | [-13.45; 13.45] | 0 | 0 |  |  | 18.00 | MF | ow/os | Mix | AL | 2.3 | 12 | 1 |
| Hollis et al, 2009 | 25 | 0.39 | 5.39 | [-10.17; 10.95] | 0 | 0 |  |  | 18.00 | MF | ow | Mix | AL | 1.5 | 12 | 1 |
| Maersket al, $2012^{*}$ | 14 | 35.19 | 7.78 | [19.94; 50.44] | 0 | 0 |  | - | 18.00 | MF | ow/os | Mix | AL | 1 | 24 | 2 |
| Hernandez-Cordero et al. 2014 | 120 | -1.00 | 1.07 | [-3.10; 1.10] | 0 | 2 |  |  | 20.00 | F | ow/os | Mix | AL | 0.5 | 36 | 2 |
| Lowndes et al, 20146* | 55 | 8.80 | 4.70 | [-2.82; 15.82] | 0 | 2 |  |  | 22.00 | MF | вм1<35 | Mix | Eu | -4.1 | 10 | 2 |
| Random effects model ( $\mathrm{r}=0.82$ ) |  | -0.30 |  | [-14.02; 13.41] |  |  |  |  |  |  |  |  |  |  |  |  |
| Hetergenety: $I^{2}=90 \%[82 \% ; 94 \%], z^{2}=309.1118, p<0.01$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Source = Foods |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Gostner et al, 2005 | 19 | -10.00 | 8.81 | [-22.98; 2.98] | 0 | 2 | - |  | 8.00 | MF | GP | Mix | Eu | 0 | 4 | 1 |
| Hallfrisch et al, 1983a* (normoinsulinemic) | 12 | 14.40 | 4.20 | [ 0.17 ; 22.63] | 0 | 0 |  | - + | 15.00 | m | $\mathrm{N}-1$ | Fruct | Eu | . | 5 | 2 |
| Halltrisch et al, 1983**(hyperinsulinemic) | 12 | 11.40 | 8.40 | [-5.08; 27.88] | 0 | 2 |  | $\square$ | 15.00 | M | H-1 | Fruct | Eu | . | 5 | 2 |
| Reiser et al, 1989a* (normoinsulinemic) | 11 | 15.08 | 6.99 | [ 1.38: 28.78 ] | 1 | 0 |  | - | 20.00 | M | $\mathrm{N}-1$ | Fruct | Eu | . | 5 | 2 |
| Reiser el al., 1989** (hyperinsulinemic) | 10 | 22.82 | 7.84 | [ 7.44: 38.19] | 1 | 0 |  | 푼 | 20.00 | M | $\mathrm{H}-1$ | Fruct | Eu | . | 5 | 2 |
| \|srael et al. 1983* | 12 | 52.00 | 8.11 | ( 36.11; 87.89 ] | 0 | 0 |  | - | 28.00 | M | $\mathrm{H}-\mathrm{I}$ | Mix | Eu | -3.8 | - | 1 |
| \|srael et al, 1983* | 12 | 21.00 | 3.31 | [14.51; 27.49] | 0 | 0 |  | + | 28.00 | F | $\mathrm{H}-1$ | Mix | Eu | 0.2 | - | 1 |
| Reiser et sl, 1979a* | 19 | 26.00 | 9.53 | [ 7.31; 44.69] | 1 | 0 |  | + | 30.00 | MF | GP | Mix | Eu | 0.5 | 6 | 2 |
| Moser et al. 1988 (OC.users) | - | 15.00 | 7.97 | [-0.82; 30.62] | 0 | 2 |  | $\pm$ | 43.00 | F | $\bigcirc$ | Mix | Eu | -1 | 4 | 1 |
| Moser et al, 1988 (No oc.users) | $\bigcirc$ | -14.00 | 12.33 | [-38.17; 10.17] | 0 | 2 |  |  | 43.00 | F | Non-OC | Mix | Eu | 1 | 4 | 1 |
| Random effects model ( $\mathrm{r}=0.82$ ) |  | 15.85 |  | [ 5.12; 26.57] |  |  |  | + |  |  |  |  |  |  |  |  |
| Heteroenerity: $I^{2}=80 \%[88 \% ; 89 \%] . \tau^{2}=241.0777, p<0.01$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Source = Mixed |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lewis et al. 2013 | 13 | 7.73 | 4.84 | [-1.38: 16.83 ] | 0 | 2 |  | $\mp$ | 10.00 | MF | ow/os | Mix | Eu | 0.7 | $\bigcirc$ | 1 |
| Markey et al. 2018 | 50 | 0.39 | 2.17 | [-3.86: 4.83] | 0 | 0 |  |  | 10.00 | MF | Non-OB | Mix | AL | 0.1 | 8 | 1 |
| Smith et sl, 1998 | 18 | 19.34 | 9.13 | [1.44: 37.23 ] | 1 | 0 |  | $\pm$ | 12.00 | MF | H-TG | Mix | AL | 2.7 | 24 | 2 |
| Bladet al. 2008 | 13 | 23.59 | 18.58 | [-12.79: 59.97] | 0 | 2 |  |  | 15.00 | M | вм1<35 | Mix | Eu | 0.4 | 8 | 1 |
| Huttunen et al, 1978 | 40 | .7.73 | 11.32 | [-29.93; 14.48] | 0 | 0 |  |  | 18.00 | MF | GP | Mix | AL |  | 72 | 2 |
| Swanson et sl, 1992 | 14 | 14.31 | 3.95 | [ 8.58 ; 22.05] | 0 | 0 |  | \# | 16.80 | MF | GP | Fruct | Eu |  | 4 | 1 |
| Saris et al, 2000* | 79 | -0.77 | 3.90 | [-8.42; 8.88] | 0 | 0 |  |  | 19.00 | MF | ow/os | Mix | AL | 0.9 | 24 | 1 |
| Umpleby et al, 2017 (No NAFLD) | 14 | 10.83 | 5.92 | [-0.77; 22.43] | 0 | 2 |  | $\square$ | 20.00 | M | OW/No-NAFLD | Mix | Eu | 2.2 | 12 | 2 |
| Umpleby et al, 2017 (NAFLD) | 11 | 13.53 | 7.32 | [-0.81; 27.88] | 0 | 2 |  | + | 20.00 | M | OWINAFLD | Mix | Eu | 2.1 | 12 | 2 |
| Raben et sl, $2002^{*}$ | 11 | -4.25 | 10.50 | (-24.83; 18.33] | , | 0 |  |  | 23.00 | MF | ow | Mix | AL | 2.8 | 10 | 1 |
| Werner et al, 1984 | 12 | 5.80 | 8.37 | (-10.80; 22.20) | 0 | 2 |  |  | 24.00 | MF | Gallstones | Mix | AL | 1.4 | 8 | 2 |
| Groen et al. 1988 | 15 | 27.00 | 8.18 | [11.00; 43.00] | 0 | 0 |  | - | 30.00 | MF | GP | Mix | Eu | -0.8 | 5 | 2 |
| Random effects model ( $\mathrm{r}=0.82)$ |  | 7.98 |  | [ 2.67; 13.28] |  |  |  |  |  |  |  |  |  |  |  |  |
| Heterogeneity: $l^{2}=00 \%[25 \% ; 79 \%] . \mathrm{z}^{2}=41.9999, p<0.01$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Random effects model ( $\mathrm{r}=0.82$ ) |  | 8.71 |  | [ 2.86; 14.56] |  |  |  | - |  |  |  |  |  |  |  |  |
| Prediction interval |  |  |  | [-21.33; 38.76] |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  | 1 | 12 |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  | $40-20$ | $20 \quad 40 \quad 60$ |  |  |  |  |  |  |  |  |
| Random effects model ( $r=0.5)$ ) $7.27[1.43 ; 13.11]$ |  |  | Blad $=$ Parallel Red $=$ Cross-over |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

Figure G.6a2: Stratified by sugars source

Figure G.6b: Effect of high vs low sugar intake on LDL-cholesterol (mg/dL)

| Study | N | Mean Effect | se Effect | 95\% CI | r 0.5 | r 0.99 |  |  | Sugar diff (E\%) | Sex | Subjects | Sugar | Source | BW* | Duration | RoB |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Diet = Isocaloric with neutral energy balance |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Gostner et 91, 2005 | 19 | -13.30 | 8.12 | [-25.30; -1.30] | 1 | 0 |  |  | 8.00 | MF | GP | Mix | f | 0 | 4 | 1 |
| Lewis et al, 2013 | 13 | 3.87 | 3.87 | [-3.32; 11.08] | 0 | 2 |  | T | 10.00 | MF | ow/ob | Mix | Mix | 0.7 | 8 | 1 |
| Lowndes et sl, 2014s | 15 | -11.80 | 8.85 | [-25.22; 1.82] | 0 | 2 | $\cdots$ |  | 10.00 | MF | оw/ob | Mix | B | 0 | 10 | 2 |
| Black et sl, 2008 | 13 | 20.50 | 8.41 | [ 7.94; 33.05] | 1 |  |  | - | 15.00 | M | вм1<35 | Mix | Mix | 0.4 | 8 | 1 |
| Hallrisch et al, 19833* ( N - HI ) | 24 | 6.90 | 4.58 | [-2.08; 15.88] | 0 | 2 |  | T- | 15.00 | M | $\mathrm{NI} \cdot \mathrm{HI}$ | Fruct | F |  | 5 | 2 |
| Swanson et sl. 1992 | 14 | 10.44 | 3.28 | [ 4.08: 16.82 ] | 1 | 0 |  | - | 18.80 | MF | GP | Fruct | Mix |  | 4 | 1 |
| Reiseret sal. 19898* (normoinsulinemic) | 11 | 12.76 | 4.90 | [ 3.15: 22.37 ] | 1 | 0 |  | $\square$ | 20.00 | M | $\mathrm{N} \cdot \mathrm{I}$ | Fruct | F |  | 5 | 2 |
| Reiser el al., 1989a*" (hyperinsulinemic) | 10 | 8.12 | 5.84 | [-2.94; 19.18] | 0 | 2 |  | F- | 20.00 | M | H-1 | Fruct | F |  | 5 | 2 |
| Umpleby et al, 2017 (No NAFLD) | 14 | 5.41 | 4.85 | [-3.69: 14.52] | $\bigcirc$ | 2 |  | 픈 | 20.00 | M | OW/No-NAFLD | Mix | Mix | 2.2 | 12 | 2 |
| Umpleby et al. 2017 (NAFLD) | 11 | 6.57 | 6.27 | [-5.71: 18.86] | 0 | 2 |  | + | 20.00 | M | OWINAFLD | Mix | Mix | 2.1 | 12 | 2 |
| Lowndes et al, 2014b* | 55 | 3.80 | 4.00 | [-4.24; 11.44] | 0 | 2 |  |  | 22.00 | MF | вм1<35 | Mix | в | -4.1 | 10 | 2 |
| lsasel et al, 1983* | 12 | 35.00 | 8.80 | [22.08: 47.94] | 0 | 0 |  | 판 | 28.00 | M | $\mathrm{H}-1$ | Mix | F | -3.8 | 8 | 1 |
| lsrase et al, 1983* | 12 | 14.00 | 3.31 | [ 7.51: 20.49] | 0 | 0 |  | ㅍ- | 28.00 | F | $\mathrm{H} \cdot \mathrm{I}$ | Mix | F | 0.2 | 8 | 1 |
| Hetergeneity: $I^{2}=75 \%[55 \%: 38 \%], z^{2}=97.9159, p<0.01$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Diet $=$ Ad libitum |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Majid et al, 2013 | 31 | -20.11 | 3.31 | [-28.80; -13.82] | 0 | 0 | $\mp$ |  | 8.00 | M | GP | Mix | B |  | 4 | 2 |
| Markey et sl, 2018 | 50 | 0.39 | 1.82 | [-3.18; 3.96] | 0 | 0 |  |  | 10.00 | MF | Non-Ob | Mix | Mix | 0.1 | 8 | 1 |
| Hollis et al, 2009 | 25 | 1.55 | 5.39 | [-9.02; 12.12] | 0 | 0 |  |  | 18.00 | MF | ow | Mix | в | 1.5 | 12 | , |
| Maersk et al. 2012* | 14 | 22.43 | 7.77 | [ 7.21: 37.85 ] | 1 | $\bigcirc$ |  | $\pm$ | 18.00 | MF | Ow/OB | Mix | B | 1 | 24 | 2 |
| Saris et al, 2000* | 79 | -2.71 | 3.35 | (-9.28: 3.88 ] | - | 0 |  |  | 19.00 | MF | Ow/os | Mix | Mix | 0.9 | 24 | 1 |
| Hernandez-Cordero et al. 2014 | 120 | -8.00 | 0.75 | [-7.47; -4.53] | 0 | 0 |  |  | 20.00 | F | OW/OB | Mix | B | 0.5 | ${ }^{36}$ | 2 |
| Werner et al, 1984 | 12 | 1.18 | 7.35 | [-13.25; 15.57] | 0 | 0 |  |  | 24.00 | MF | Gallstones | Mix | Mix | 1.4 | 6 | 2 |
| Random effects model ( $\mathrm{r}=0.82$ ) |  | -1.66 |  | [-10.17; 6.84] |  |  |  |  |  |  |  |  |  |  |  |  |
| Hetergenerity: $l^{2}=87 \%[78 \% ; 93 \%) \cdot z^{2}=111.0518, p<0.01$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Random effects model ( $\mathrm{r}=0.82$ ) |  | 4.49 |  | [-0.88; 9.87] |  |  |  | + |  |  |  |  |  |  |  |  |
| Prediction interval [-19.76; 28.75] |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  | 1 |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  | -20 | $20 \quad 40$ |  |  |  |  |  |  |  |  |
| Random effects model ( $r=0.5)$ : $3.38[-2.03 ; 8.75]$ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Random effects model ( $r=0.99)$ : $4.91[-0.88$; |  |  |  | $=1 \gg$ significant | d (0.82 | comes | significan: | $\begin{aligned} & \text { Red }=\text { Cross-over } \\ & 5) ; ~ r o .99=2->\text { non sig } \end{aligned}$ | ant effect (0.82) b | mes | ificant (0.99) |  |  |  |  |  |

Figure G.6b1: Stratified by type of diet


Figure G.6b2: Stratified by sugars source

Figure G.6c: Effect of high vs low sugar intake on HDL-cholesterol (mg/dL)


Figure G.6c1: Stratified by type of diet

