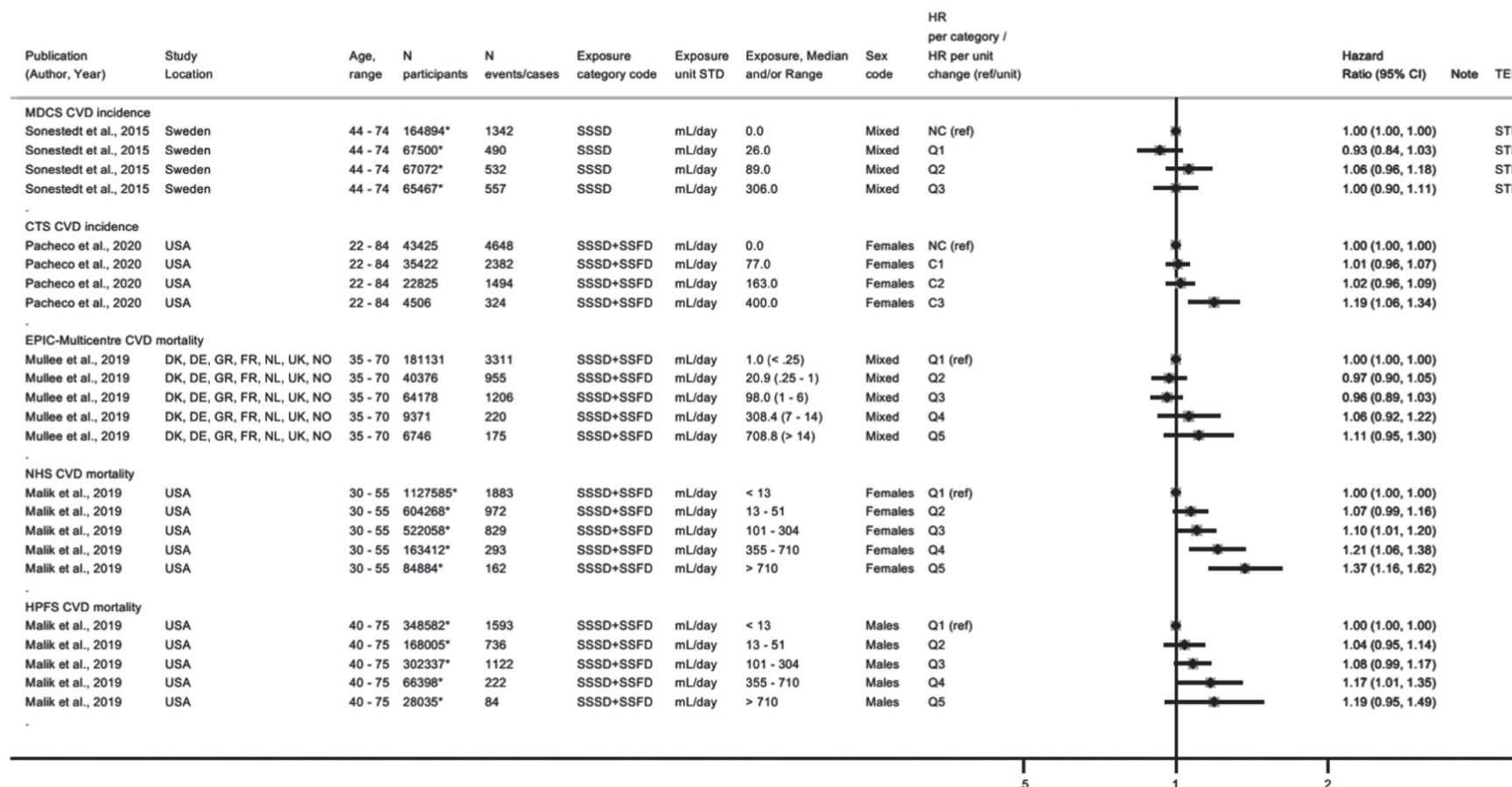


Figure K.17: Intake of SSBs and incidence and mortality of cardiovascular diseases

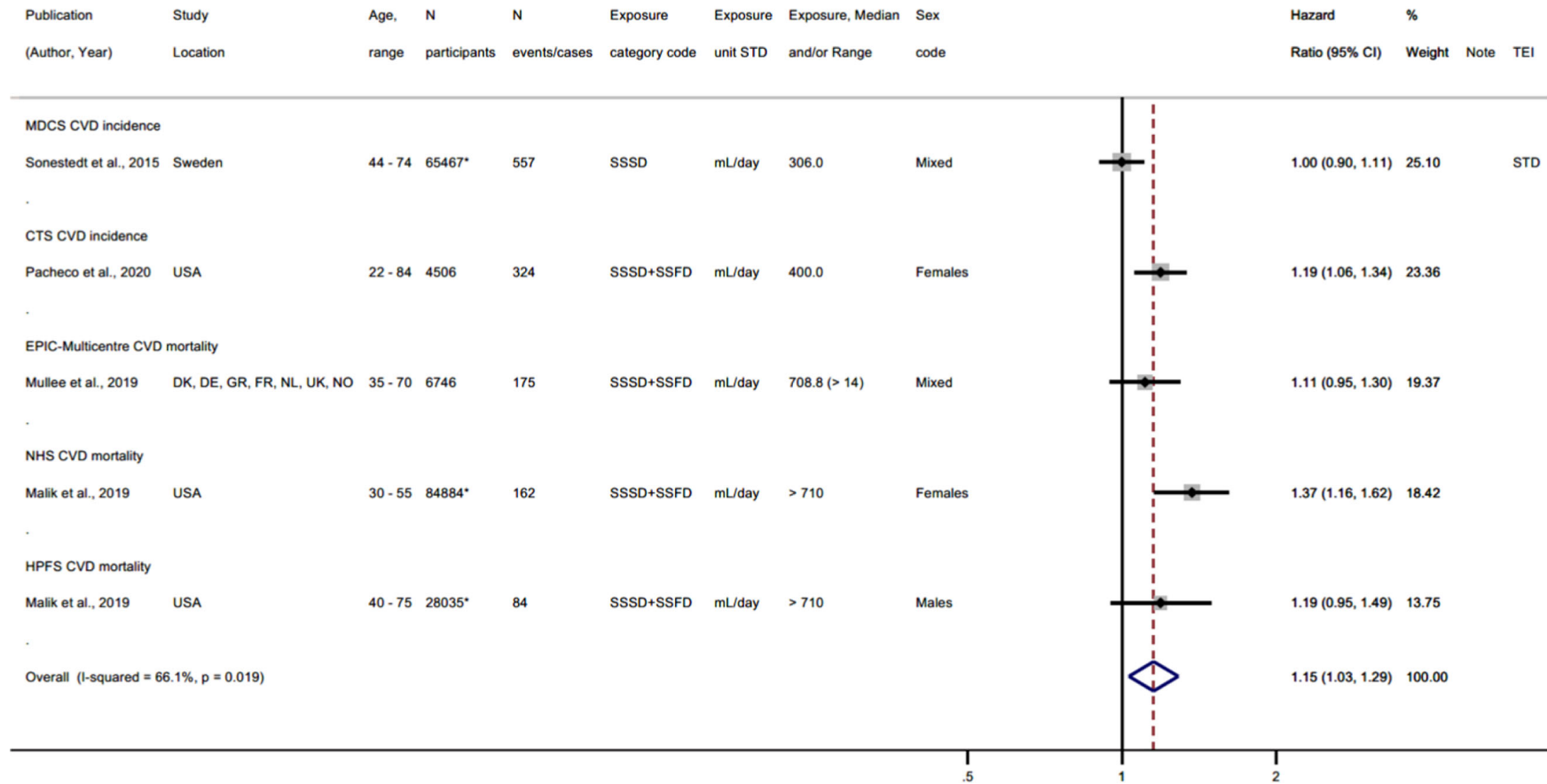
HRs from MOST ADJ models sorted by increasing exposure



Note: STD = Standardised for Total Energy Intake; *=Person-years.

Figure K.17a1: Intake of SSBs and cardiovascular disease (composite endpoint) incidence and mortality – General plot

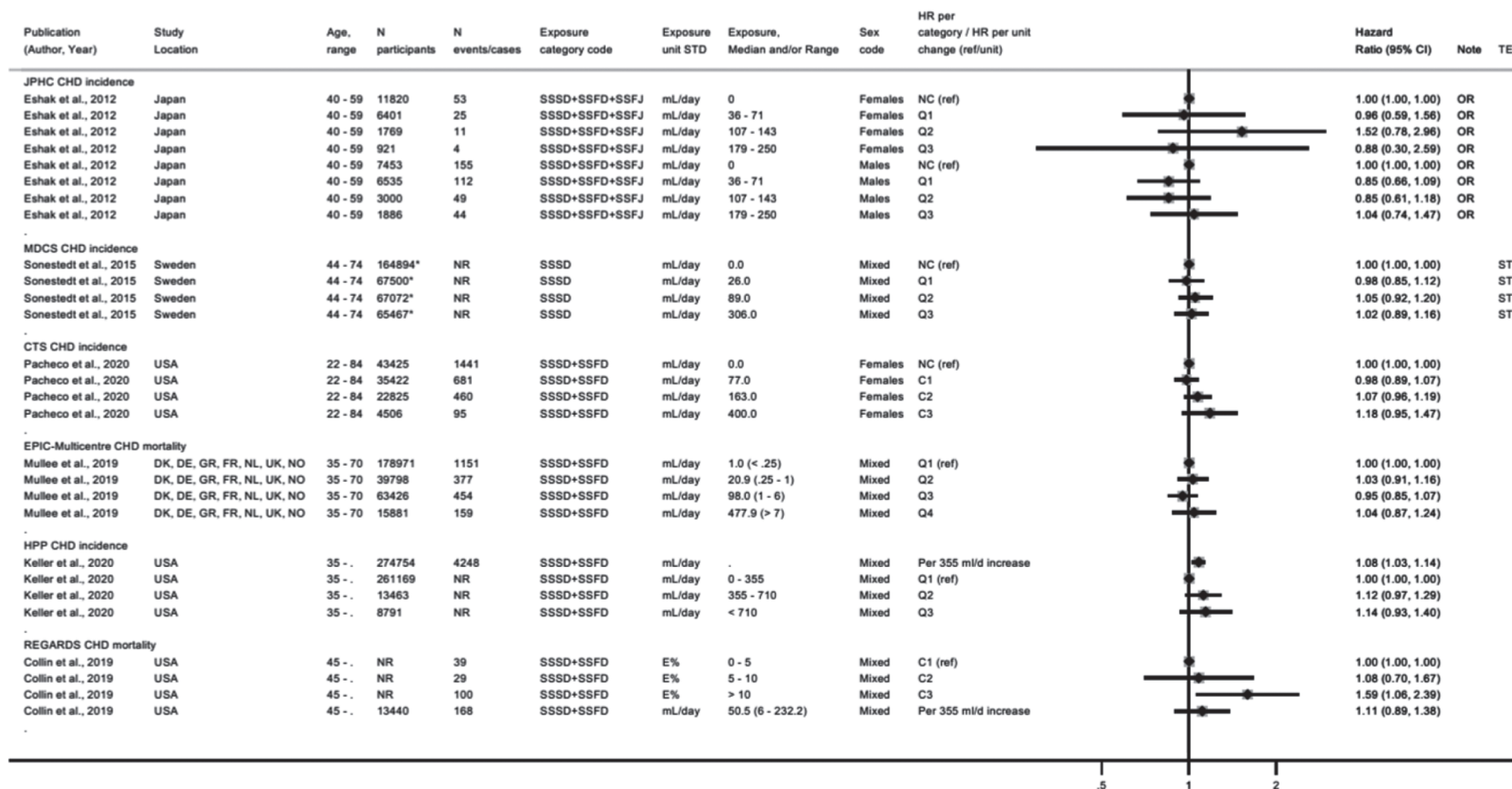
Highest vs. Lowest HRs from MOST ADJ models sorted by increasing exposure



Note: STD = Standardised for Total Energy Intake; *=Person-years.

Figure K.17a2: Intake of SSBs and cardiovascular disease (composite endpoint) incidence and mortality – Pooled plot

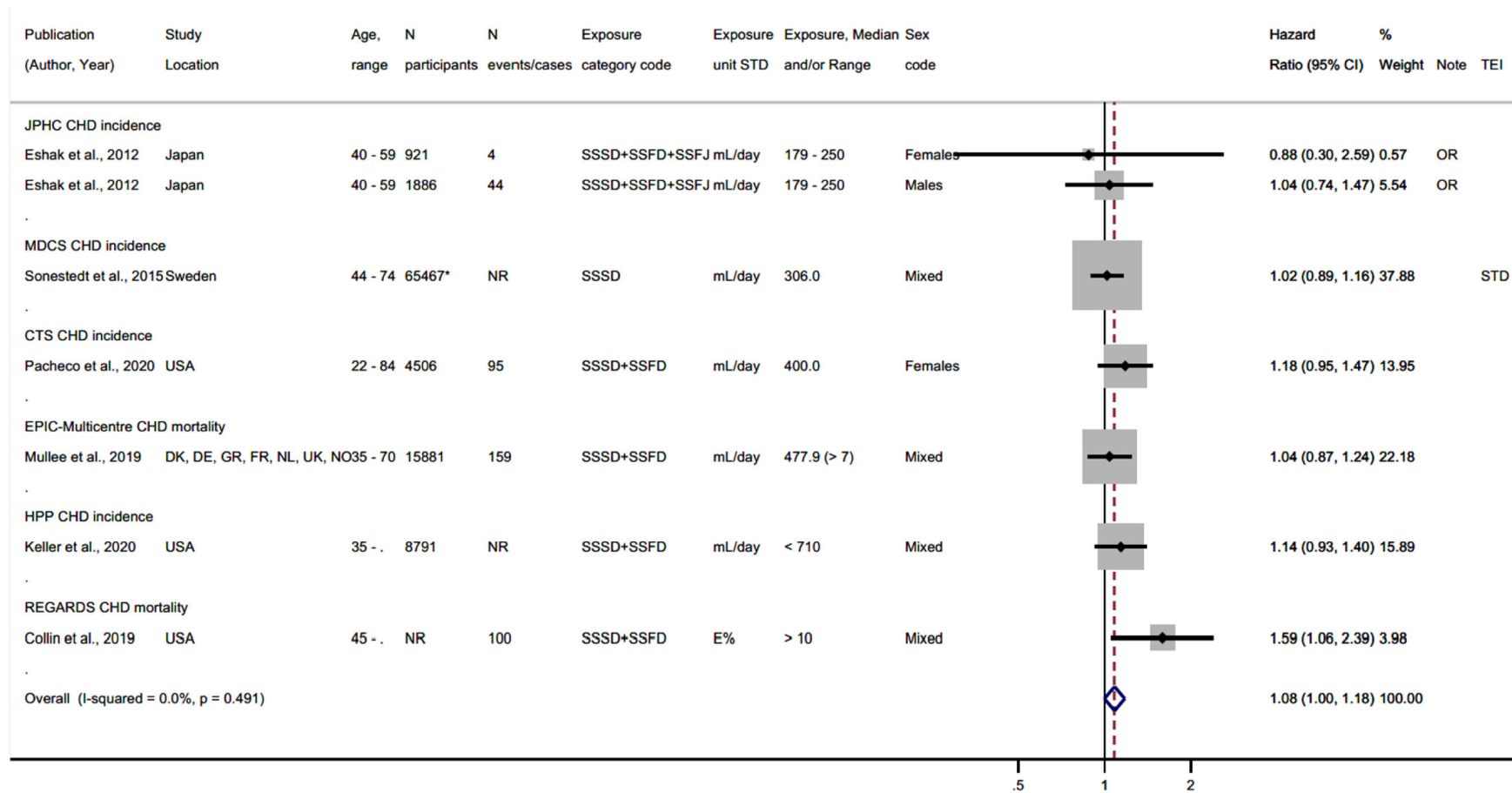
HRs from MOST ADJ models sorted by increasing exposure



Note: OR = Odds Ratio; STD = Standardised for Total Energy Intake; *=Person-years.

Figure K.17b1: Intake of SSBs and coronary heart disease incidence and mortality – General plot

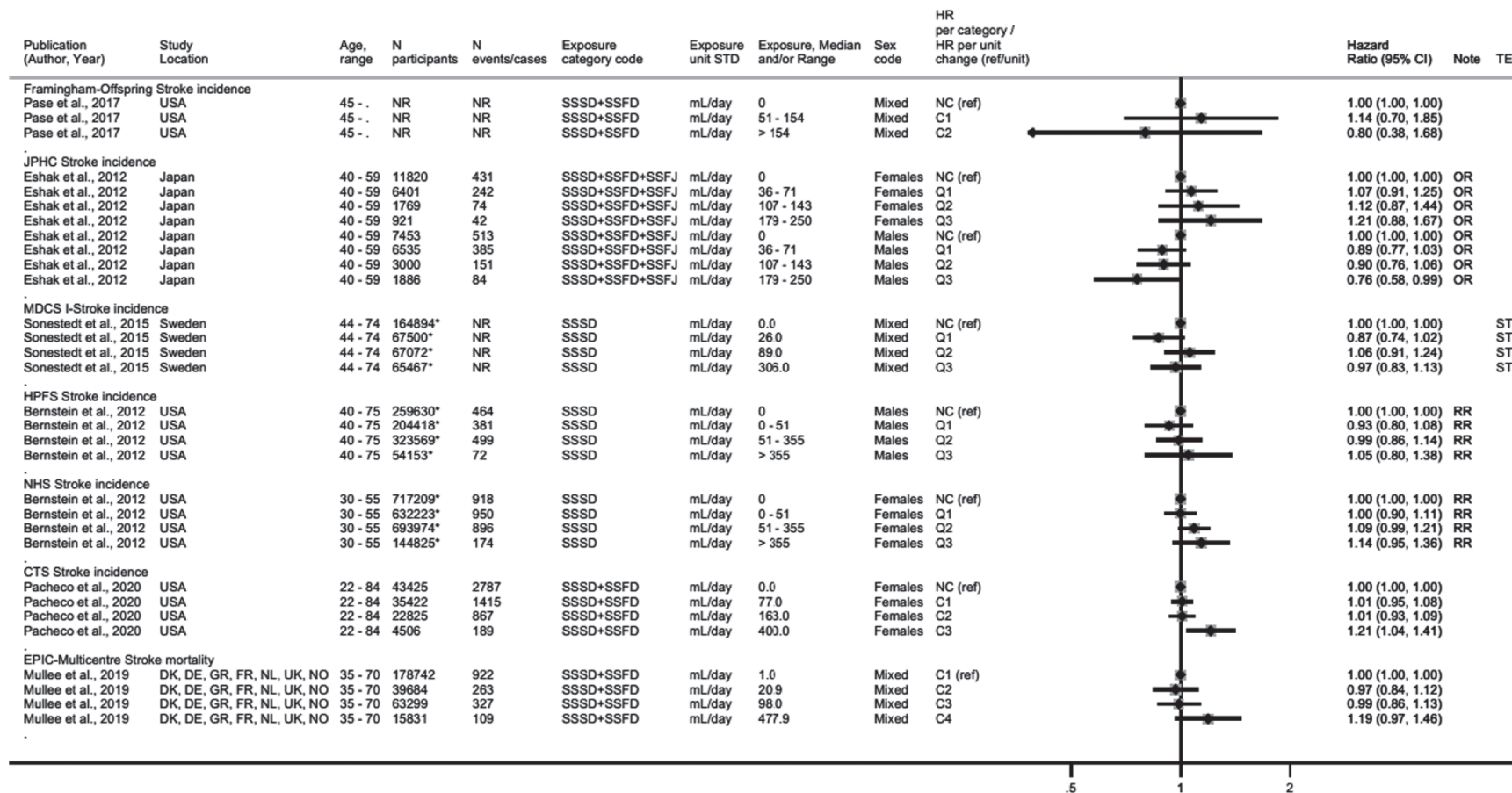
Highest vs. Lowest HRs from MOST ADJ models sorted by increasing exposure



Note: OR = Odds Ratio; STD = Standardised for Total Energy Intake; *=Person-years.

Figure K.17b2: Intake of SSBs and coronary heart disease incidence and mortality – Pooled plot

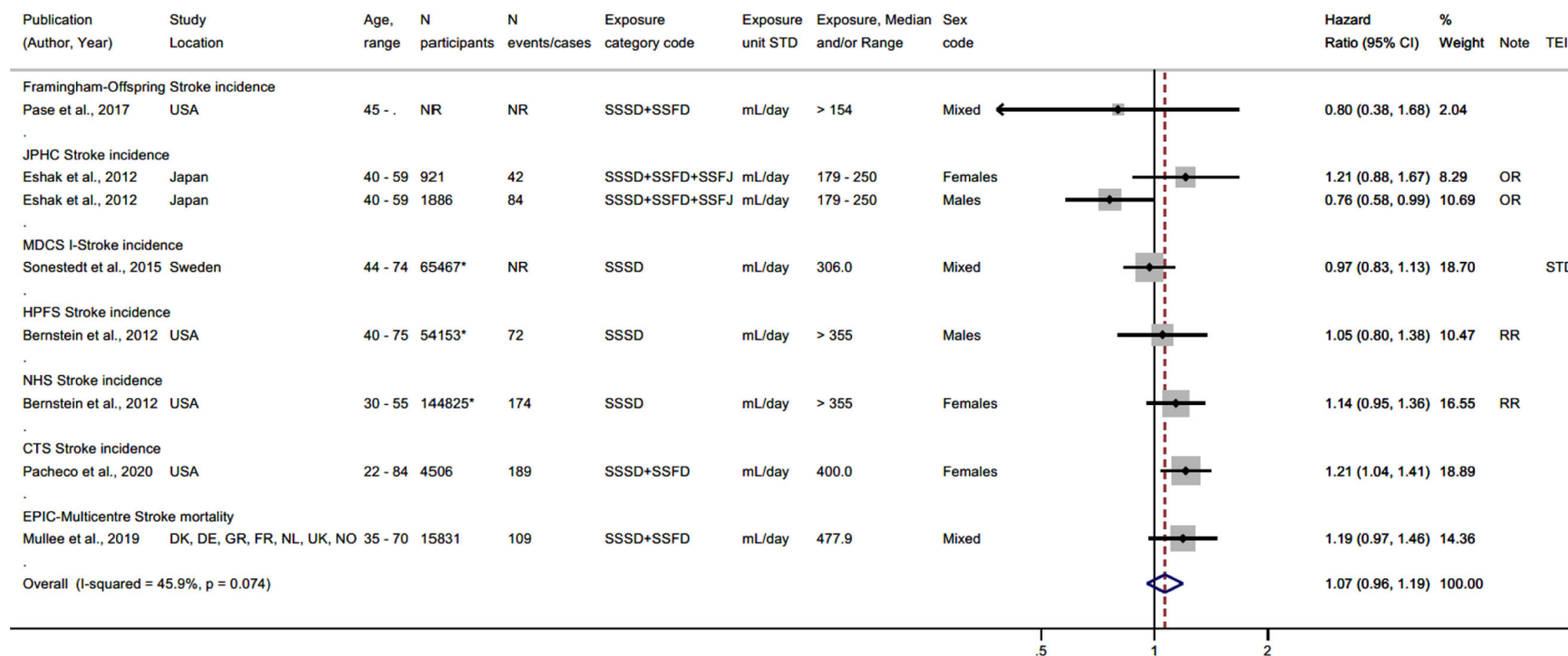
HRs from MOST ADJ models sorted by increasing exposure



Note: OR = Odds Ratio; RR= Rate ratio; STD = Standardised for Total Energy Intake; *=Person-years; in Framingham-Offspring cohort (Pase et al., 2017) exposure = cumulative intake.

Figure K.17c1: Intake of SSBs and stroke incidence and mortality – General plot

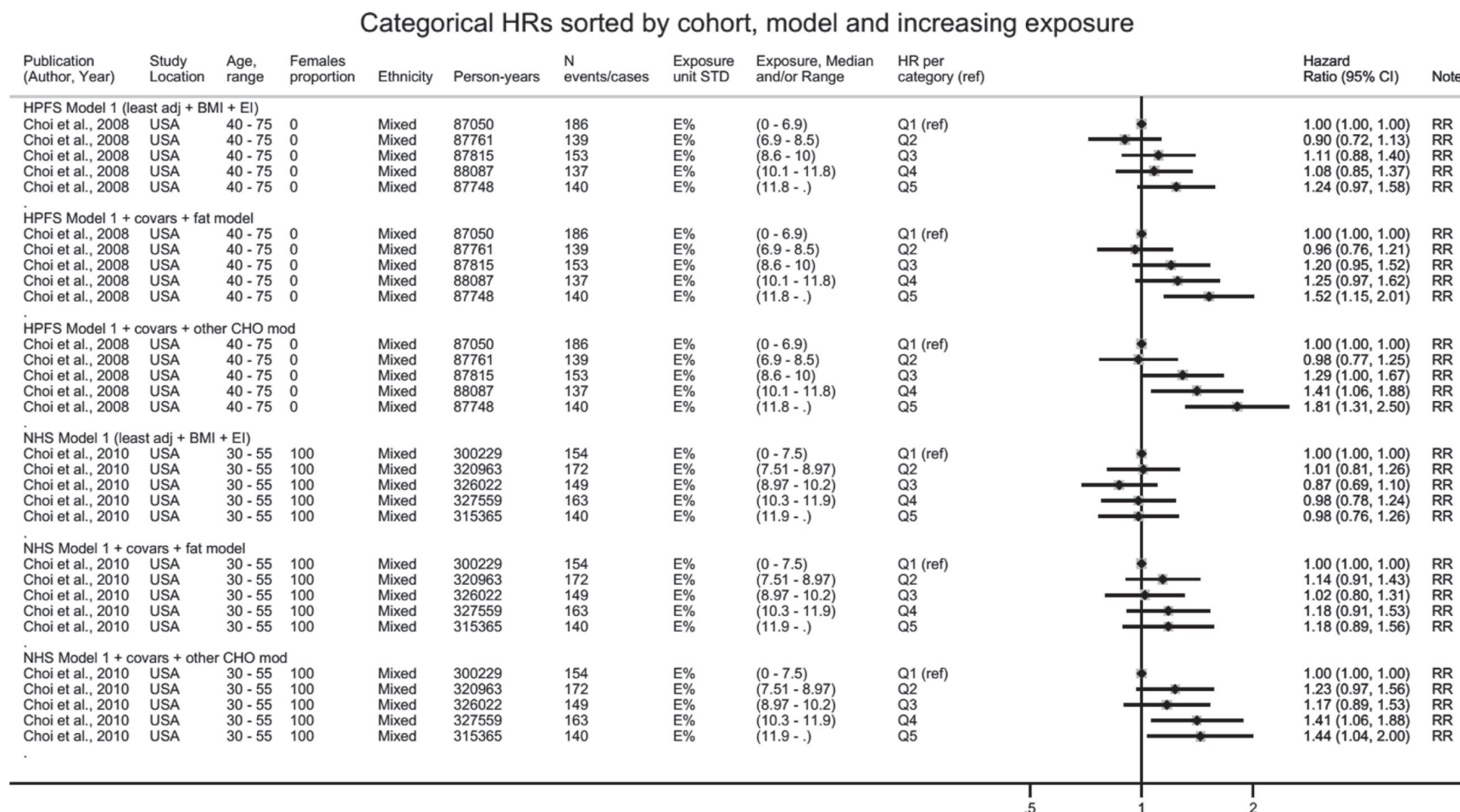
Highest vs. Lowest HRs from MOST ADJ models sorted by increasing exposure



Note: OR = Odds Ratio; RR= Rate ratio; STD = Standardised for Total Energy Intake.

Figure K.17c2: Intake of SSBs and stroke incidence and mortality – Pooled plot

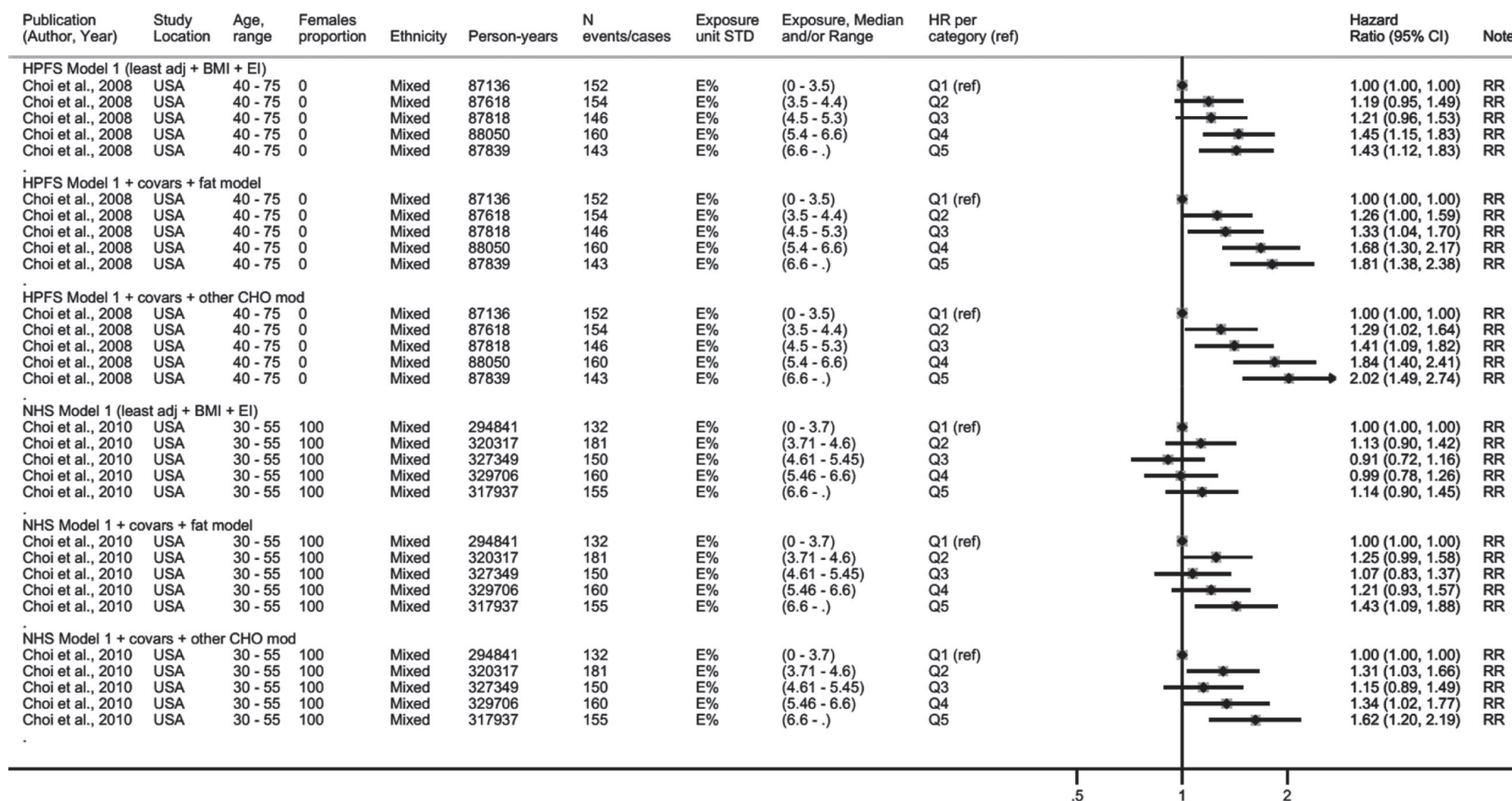
Figure K.18: Fructose and incidence of gout



Note: RR= Rate ratio.

Figure K.18a: Total fructose and incidence of gout

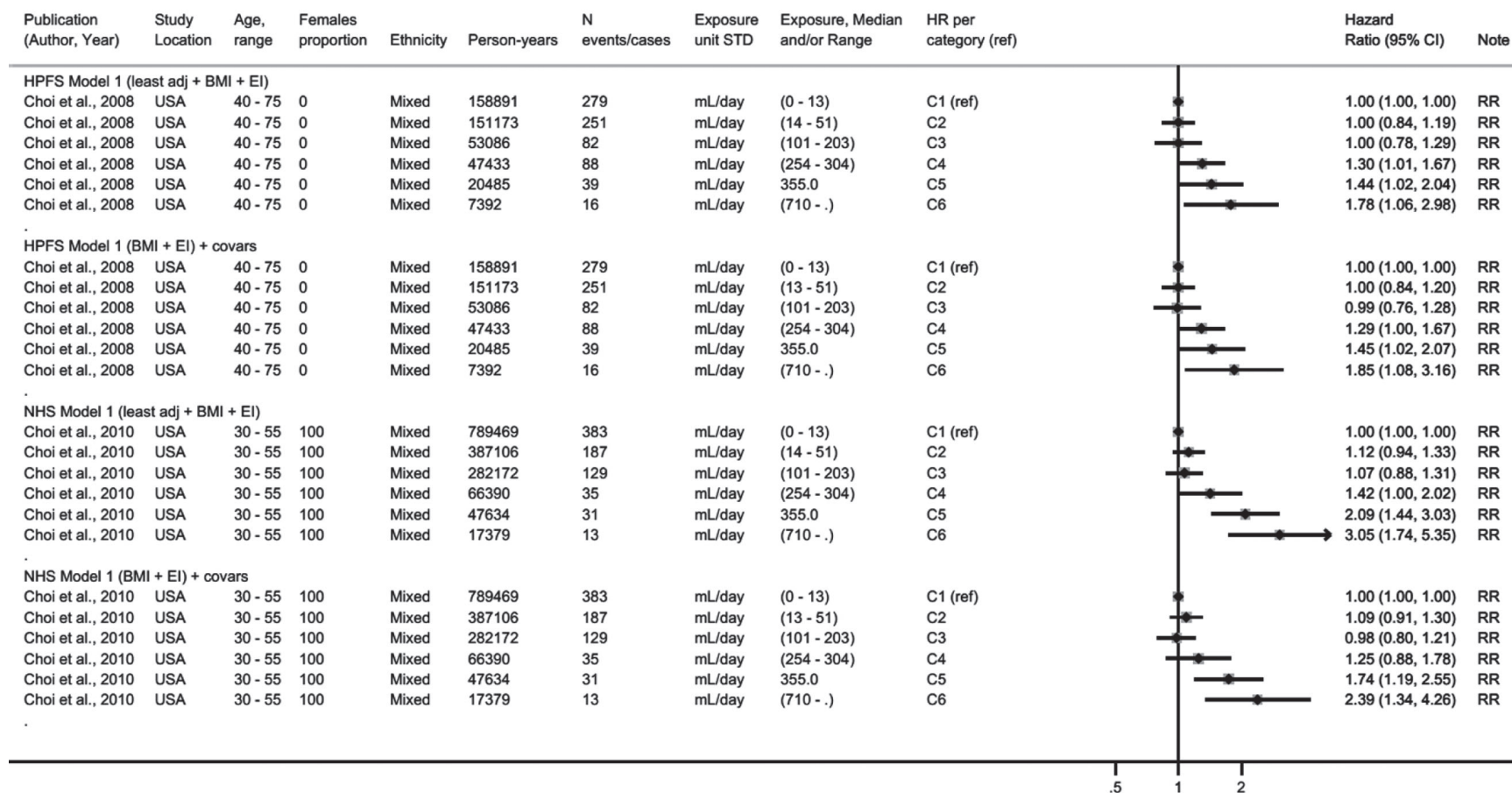
Categorical HRs sorted by cohort, model and increasing exposure



Note: RR= Rate ratio.

Figure K.18b: Free fructose and incidence of gout

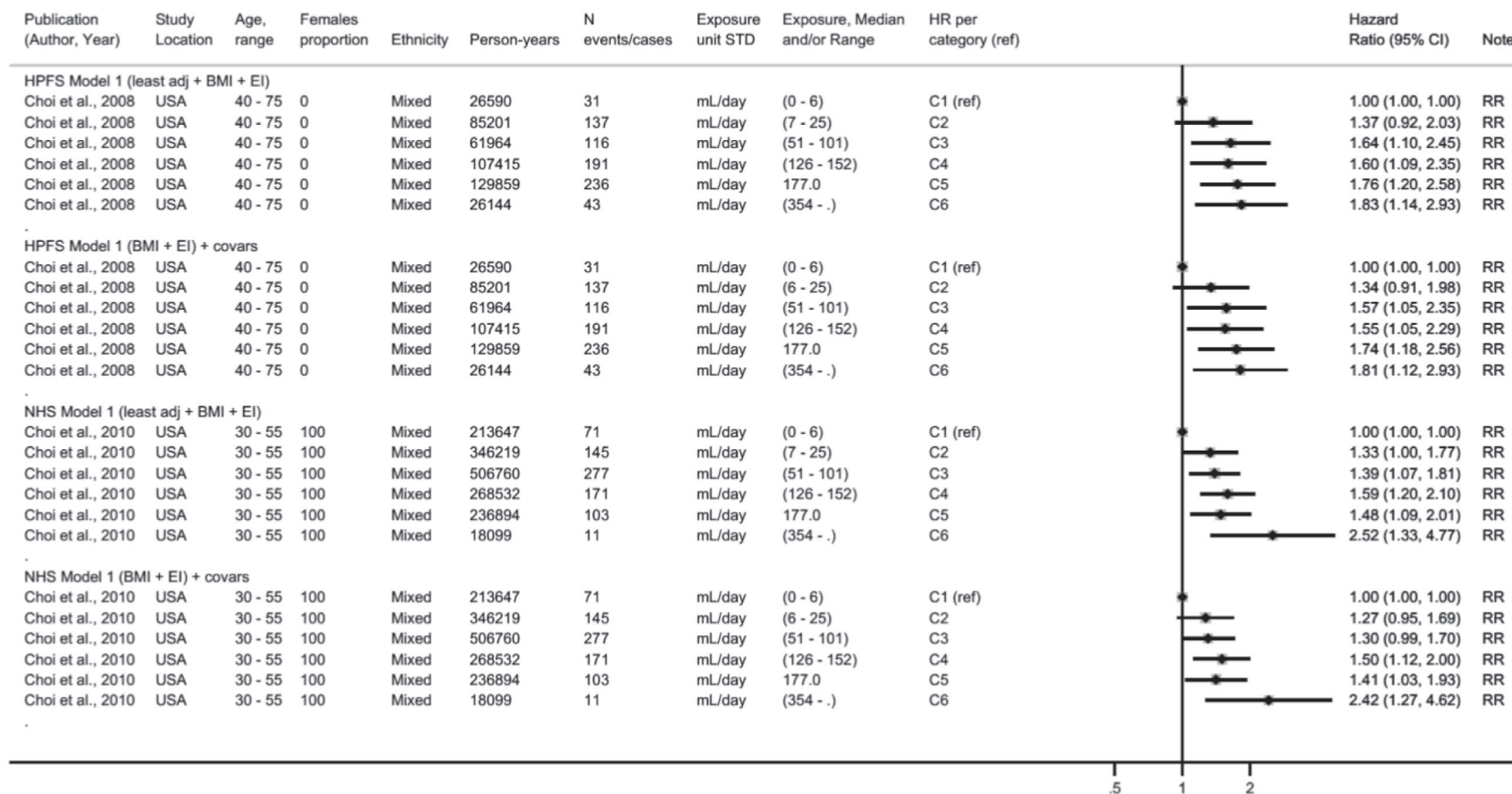
Categorical HRs sorted by cohort, model and increasing exposure



Note: RR= Rate ratio

Figure K.19: SSBs and incidence of gout

Categorical HRs sorted by cohort, model and increasing exposure



Note: RR= Rate ratio

Figure K.20: Fruit juices and incidence of gout

Appendix L – Summary of risk of bias ratings for observational studies by endpoint

Table L.1a: Added and free sugars and continuous variables related to the risk of obesity and abdominal obesity

| Cohort | Outcome | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|--------------|-------------|-------------|----------|---------|-----------|-----------------------|------|
| DONALD | BMIz | -/NR | + | ++ | -/NR | + | 2 |
| EPIC-Norfolk | BMI; WC | -/NR | + | ++ | -/NR | ++ | 2 |
| KoCAS | BMIz | -- | -/NR | + | -/NR | + | 3 |
| Mr and Ms OS | BW; BMI | -/NR | + | + | + | -/NR | 2 |
| NGHS | BMIz; WC | + | + | ++ | -/NR | + | 1 |
| NSHDS | BMI | - | + | + | -/NR | + | 2 |
| PHHP | BW | -/NR | + | + | -/NR | -/NR | 2 |
| QUALITY | BW; BMI; WC | + | + | + | -/NR | + | 1 |

Table L.1b: Added and free sugars and measures of body fat and abdominal fat

| Cohort | Outcome | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|--------------|-----------------------|-------------|----------|---------|-----------|-----------------------|------|
| DONALD | BF (%) | -/NR | + | -/NR | -/NR | + | 3 |
| KoCAS | BF (%) | -- | -/NR | -- | -/NR | + | 3 |
| Mr and Ms OS | BF (% and kg) | -/NR | + | ++ | + | -/NR | 2 |
| Mr and Ms OS | Central fat mass (kg) | -/NR | + | + | + | -/NR | 2 |
| QUALITY | BF (kg) | + | + | ++ | -/NR | + | 1 |

Table L.2: SSBs and incidence of obesity

| Cohort | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|--------------|-------------|----------|---------|-----------|-----------------------|------|
| Amsterdam | - | -/NR | -/NR | -/NR | + | 3 |
| BWHS | + | + | + | + | + | 1 |
| DDHP | - | - | ++ | + | ++ | 2 |
| ELEMENT | -/NR | -/NR | ++ | -/NR | + | 3 |
| Generation-R | + | -/NR | ++ | -/NR | ++ | 2 |
| PHI | + | -/NR | + | -/NR | ++ | 2 |

Table L.3: SSBs and incidence of abdominal obesity

| Cohort | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|---------|-------------|----------|---------|-----------|-----------------------|------|
| CARDIA | + | + | ++ | -/NR | + | 1 |
| ELEMENT | -/NR | -/NR | ++ | -/NR | + | 3 |
| Girona | + | + | + | -/NR | + | 1 |
| KoGES | + | -/NR | ++ | -/NR | + | 2 |
| TLGS | -/NR | -/NR | -/NR | -/NR | -/NR | 3 |

Table L.4a: SSBs and continuous variables related to the risk of obesity and abdominal obesity

| Cohort | Outcome | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|-----------------|---------------------------|-------------|----------|---------|-----------|-----------------------|------|
| AGAHLS | BMI | -/NR | -/NR | ++ | -/NR | -/NR | 3 |
| ALSPAC | BW; BMI; WC | ++ | + | + | + | ++ | 1 |
| CoSCIS | BMI | -/NR | + | + | -/NR | ++ | 2 |
| DCH | BW; WC; WC _{BMI} | -/NR | -/NR | -/NR | + | ++ | 3 |
| DONALD | BMI | -/NR | + | ++ | + | + | 1 |
| EPIC-Diogenes | WC _{BMI} | -/NR | -/NR | -/NR | -/NR | ++ | 3 |
| Framingham-3Gen | BW | + | -/NR | + | + | ++ | 1 |
| GUTS | BMI | -/NR | + | -/NR | + | -/NR | 3 |
| GUTSII | BMI | -/NR | + | -/NR | -/NR | ++ | 3 |
| HPFS | BW | + | + | + | + | ++ | 1 |
| HSS-DK | BW; BMIz | + | + | ++ | + | ++ | 1 |
| Inter99 | BW; WC; WC _{BMI} | -/NR | -/NR | + | -/NR | ++ | 3 |
| MIT-GDS | BMI | -/NR | -/NR | + | + | ++ | 2 |
| MONICA | BW | -/NR | -/NR | + | -/NR | ++ | 3 |
| MOVE | BMI | - | -/NR | + | + | + | 2 |
| MTC | BW; WC | + | + | -/NR | -/NR | + | 2 |
| NGHS | BMI | -/NR | + | + | + | -/NR | 2 |
| NHS | BW | + | + | + | + | ++ | 1 |
| NHS II | BW | + | + | + | + | ++ | 1 |
| SUN | BW | + | + | -/NR | + | + | 1 |
| WAPCS | BMI | + | + | + | -/NR | + | 1 |
| WAPCS | WC | + | + | -/NR | -/NR | + | 2 |
| WHI | BW | + | + | + | -/NR | ++ | 1 |

WC_{BMI} = WC regressed on BMI.

Table L.4b: SSBs and measures of body fat and abdominal fat

| Cohort | Outcome | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|-----------------------|---------------|-------------|----------|---------|-----------|-----------------------|------|
| AGAHLS | BF (%) | -/NR | -/NR | ++ | -/NR | + | 3 |
| AGAHLS | Trunk fat (%) | -/NR | -/NR | + | -/NR | -/NR | 3 |
| ALSPAC ⁽¹⁾ | BF (kg) | ++ | + | ++ | + | ++ | 1 |
| ALSPAC ⁽²⁾ | BF (kg) | + | + | ++ | -/NR | + | 1 |
| CoSCI | BF (log SFT) | -/NR | + | + | -/NR | ++ | 2 |
| DONALD | BF (%) | -/NR | + | -/NR | + | + | 2 |
| MIT-GDS | BF (%) | -/NR | -/NR | - | + | ++ | 3 |
| MOVE | BF (%) | - | -/NR | - | + | + | 3 |

(1): Bigornia et al. (2015).

(2): Johnson et al. (2007).

Table L.5: FJs and continuous variables related to the risk of obesity

| Cohort | Outcome | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|----------------|-------------------|-------------|----------|---------|-----------|-----------------------|------|
| EPIC-DiOGenes* | WC _{BMI} | -/NR | -/NR | -/NR | -/NR | ++ | 3 |
| DONALD | BMI | -/NR | + | ++ | + | + | 1 |
| GUTS | BMIz | -/NR | + | -/NR | + | + | 2 |
| HPFS | BW | + | + | + | + | ++ | 1 |
| MOVE | BMI | - | -/NR | + | + | + | 2 |
| NGHS | BMI | -/NR | + | + | + | -/NR | 2 |
| NHS | BW | + | + | + | + | ++ | 1 |
| NHS II | BW | + | + | + | + | ++ | 1 |
| Project Viva | BMIz | -/NR | -/NR | ++ | -/NR | + | 3 |
| WHI | BW | + | + | + | -/NR | ++ | 1 |

WC_{BMI} = WC regressed on BMI.

Table L.6 : Total sugars and incidence of T2DM

| Cohort | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|---------------|-------------|----------|---------|-----------|-----------------------|------|
| EPIC-InterAct | -/NR | + | + | -/NR | ++ | 2 |
| FMCHES | + | + | ++ | ++ | ++ | 1 |
| WHI | ++ | ++ | -/NR | NR | ++ | 2 |
| WHS | + | + | -/NR | + | + | 1 |

Table L.7 : Sucrose and incidence of T2DM

| Cohort | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|--------------|-------------|----------|---------|-----------|-----------------------|------|
| EPIC-Norfolk | + | + | -/NR | + | ++ | 1 |
| FMCHES | + | + | ++ | ++ | ++ | 1 |
| MDCS | - | + | + | ++ | -/NR | 2 |
| WHS | + | + | -/NR | + | + | 1 |

Table L.8: SSBs and incidence of T2DM

| Cohort | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|----------------------|-------------|----------|---------|-----------|-----------------------|------|
| ARIC | + | -/NR | + | + | ++ | 1 |
| BWHS | + | + | -/NR | + | + | 1 |
| CARDIA | -/NR | + | ++ | -/NR | + | 2 |
| EPIC-InterAct | -/NR | -/NR | + | + | ++ | 2 |
| FMCHES | + | -/NR | ++ | ++ | -/NR | 2 |
| Framingham-Offspring | -/NR | + | + | + | ++ | 1 |
| HPFS | + | + | -/NR | + | ++ | 1 |
| JPHC | + | + | -/NR | -/NR | + | 2 |
| KoGES | -/NR | -/NR | ++ | -/NR | + | 3 |
| MDCS | - | -/NR | + | ++ | -/NR | 3 |
| NHS II | + | + | -/NR | NR | ++ | 2 |
| TLGS | + | -/NR | + | -/NR | -/NR | 2 |
| Toyama | + | -/NR | ++ | ++ | + | 1 |
| WHI | + | -/NR | -/NR | NR | + | 3 |

Table L.9: FJs and incidence of T2DM

| Cohort | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|---------------|-------------|----------|---------|-----------|-----------------------|------|
| BWHS | + | + | -/NR | + | + | 1 |
| CARDIA | -/NR | + | ++ | -/NR | + | 2 |
| EPIC-InterAct | -/NR | -/NR | + | + | ++ | 2 |
| HPFS | + | + | -/NR | ++ | + | 1 |
| JPHC | + | -- | -/NR | -/NR | + | 3 |
| NHS | + | + | -/NR | NR | + | 2 |
| NHS II | + | + | -/NR | NR | + | 2 |
| SUN | + | + | -/NR | -/NR | + | 2 |
| WHI | + | + | -/NR | + | + | 1 |

Table L.10: SSBs and incidence of dyslipidaemia

| Cohort | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|-----------------------|-------------|----------|---------|-----------|-----------------------|------|
| CARDIA | -/NR | + | ++ | -/NR | + | 2 |
| Framingham-3Gen‡ | + | -/NR | + | -/NR | ++ | 2 |
| Framingham-Offspring‡ | + | + | + | + | ++ | 1 |
| KoGES | -/NR | -/NR | ++ | -/NR | + | 3 |
| TLGS | + | -/NR | ++ | -/NR | -/NR | 2 |

‡: Study identified through an update of the literature search.

Table L.11 : SSBs and incidence of hypertension

| Cohort | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|--------|-------------|----------|---------|-----------|-----------------------|------|
| CARDIA | + | + | ++ | -/NR | + | 1 |
| HPFS | + | + | + | + | + | 1 |
| KoGES | ++ | -/NR | ++ | -/NR | + | 2 |
| NHS | + | + | + | + | + | 1 |
| NHS II | + | + | + | + | + | 1 |
| SUN | + | + | -/NR | + | ++ | 1 |
| TLGS | -/NR | -/NR | + | -/NR | -/NR | 3 |

Table L.12 : Total sugars and incidence and/or mortality of cardiovascular diseases

| Cohort | Outcome | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|-------------------|--|-------------|----------|---------|-----------|-----------------------|------|
| EPIC-Multicentre‡ | CHD | + | + | + | + | ++ | 1 |
| EPIC-Morgen | Stroke | + | + | + | + | ++ | 1 |
| EPICOR | Stroke | + | + | + | ++ | + | 1 |
| EPIC-Utrecht | CVD; Stroke | ++ | + | + | + | + | 1 |
| NIH-AARP | CVD | + | + | -/NR | ++ | + | 1 |
| SCHS | CHD | + | + | -/NR | ++ | ++ | 1 |
| Takayama‡ | CVD | + | -/NR | -/NR | + | + | 2 |
| WHI | CVD; CHD; Stroke; Heart failure; CABG; PCI | ++ | + | -/NR | NR | ++ | 2 |

‡: Study identified through an update of the literature search.

Table L.13: Fructose and incidence and/or mortality of cardiovascular diseases

| Cohort | Outcome | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|-----------|---------|-------------|----------|---------|-----------|-----------------------|------|
| NIH-AARP | CVD | + | + | -/NR | ++ | + | 1 |
| TLGS | CVD | -/NR | -/NR | -/NR | NR | -/NR | 3 |
| Takayama‡ | CVD | + | -/NR | -/NR | + | + | 2 |

‡: Study identified through an update of the literature search.

Table L.14 : SSBs and incidence and/or mortality of cardiovascular diseases

| Cohort | Outcome | Confounding | Exposure | Outcome | Attrition | Other sources of bias | Tier |
|----------------------|-------------------|-------------|----------|---------|-----------|-----------------------|------|
| CTS‡ | CVD; CHD; Stroke | + | -/NR | -/NR | ++ | ++ | 2 |
| CTS‡ | Revascularisation | + | -/NR | + | ++ | ++ | 1 |
| EPIC-Multicentre‡ | CVD; CHD; Stroke | -/NR | -/NR | -/NR | ++ | ++ | 3 |
| HPFS | Stroke | + | + | -/NR | + | ++ | 1 |
| HPFS‡ | CVD | + | ++ | + | -/NR | ++ | 1 |
| HPP‡ | CHD | + | -/NR | -/NR | ++ | ++ | 2 |
| JPHC | CHD; Stroke | + | + | -/NR | ++ | ++ | 1 |
| MDCS | CVD; CHD; Stroke | + | -/NR | + | ++ | ++ | 1 |
| NHS | Stroke | + | + | -/NR | + | ++ | 1 |
| NHS‡ | CVD | + | ++ | + | -/NR | ++ | 1 |
| REGARDS‡ | CHD | -/NR | -/NR | + | -/NR | + | 3 |
| Framingham-Offspring | Stroke | + | ++ | ++ | -/NR | + | 1 |

‡: Study identified through an update of the literature search.

Appendix M – Observational studies on dental caries

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person-years | Outcome measure | Model covariates | Results |
|-------------------------------|---|---|---|---|---|---|--|--|
| Exposure: total sugars | | | | | | | | |
| 1 | Finnish cohort Bernabé et al. (2016) Finland Up to 11 years Public funding | N = 6,335 Population sampled: General population Excluded: being edentate, lack of caries outcome in at least 2 of the three surveys (2000, 2004 and 2011), missing data on covariates. n = 1,702 Sex: 56% females Ethnicity: Caucasian Age: 30–89 years | DMFT index increment DMFT index = sum of decayed, missing and filled teeth Identical clinical oral examinations were conducted at baseline and follow-ups by dentists. The overall kappa value for inter- and intra-examiner reliability at the baseline survey was 0.87 and 0.95 at tooth level, respectively. | SFFQ of 128 food items and mixed dishes – previous year SFFQ only administered at baseline. Standard portion size assigned to each FFQ item and specified with natural units The overall frequency of sugars intake (times/day) was estimated by adding the weighted responses for 15 sugary food items The amount of sugars intake (g/day) was estimated by multiplying the food consumption frequency by fixed portion sizes. The ingredients of mixed foods were broken down into their components as well as the contents of different nutrients via | Amount (g/day) (mean ± SD; range) Frequency (times/day) (mean ± SD; range) | Mean DMFT units (95%CI) increase from baseline 2004: 0.47 (0.37, 0.58) 2011: 0.74 (0.64, 0.84) | Model 1: crude Model 2: sex, age and education Model 3: model 2 + dental behaviours (toothbrushing frequency, dental attendance pattern and use of fluoride toothpaste) Model 4: model 3 + mutual adjustment for amount of sugar intake and frequency of intake, respectively | DMFT units increment (95%CI) Amount, for each 10 g/day of TS intake Model 1 0.06 (0.00, 0.12); P = 0.055 Model 2 0.10 (0.04, 0.15); P: < 0.001 Model 3 0.10 (0.04, 0.15); P: < 0.001 Model 4 0.09 (0.02, 0.15); P = 0.014 Frequency, for each time/day Model 1 0.10 (–0.0, 0.22); P = 0.101 Model 2 0.14 (0.03, 0.24); P = 0.011 Model 3 0.15 (0.04, 0.25); P = 0.007 Model 4 0.03 (–0.10, 0.17); P = 0.628 |

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person-years | Outcome measure | Model covariates | Results |
|----------|--|--|---|--|--|---|--|--|
| | | | | the Finnish Food Composition Database. | | | | A level of intake of total sugars associated with a zero increment in the DMFT index could not be identified** |
| 3 | VA-DLS Kaye et al. (2015)* USA 11 ± 5 years (mean) Public funding | N = 687 Population sampled: U.S Veterans from greater Boston area Excluded: less than 2 teeth at first examination, no follow-up examination, no teeth with an exposed root surface, missing dietary data (baseline in 1987, end of follow-up. Examinations every 2 to 4 years) n = 533 Sex: men Age: 47–90 years | Adjusted root caries increment A single calibrated periodontist examiner performed clinical assessments. An exposed root surface was considered at risk for caries if recession was 2 mm or greater. Full-mouth intraoral radiographs were taken at | Repeated administration of an expanded self-administered 131-item SFFQ at each visit. Validation against two 7-day diet records administered 6 months apart. ^{65,66} The SFFQ was administered twice to 127 men at one-year interval. Average dietary variables were computed from all SFFQs after the first root surface was exposed until edentulism or the end of the study for | E% (range) Q1: 3.8–15.0 Q2: 15.1–17.9 Q3: 18.0–20.4 Q4: 20.5–36.7 n Q1: 130 Q2: 133 Q3: 134 Q4: 136 | Teeth with new root caries events (mean ± SD (range)): 2.6 ± 2.9 (0–23) Teeth with reversals: 1.1 ± 1.5 (0–10) | Model: years at risk of root caries and baseline values of age, smoking status, number of teeth at risk for root caries, existing root caries/restorations, subgingival calculus on one or more surfaces, dental prophylaxis in past year and removable denture | Adjusted Root Caries Increment, mean (95%CI) Q1: 2.60 (2.05, 3.31) Q2: 2.64 (2.07, 3.36) Q3: 2.56 (2.01, 3.27) Q4: 2.51 (1.98, 3.18) P per trend NS |

⁶⁵ Rimm EB, Giovannucci EL, Stampfer MJ et al. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. *Am J Epidemiol* 1992;135:1114–1126.

⁶⁶ Feskanich D, Rimm EB, Giovannucci EL, et al. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. *J Am Diet Assoc.* 1993;93:790–796.

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person- years | Outcome measure | Model covariates | Results |
|----------|--|---|---|---|---|--|--|---|
| | | | each examination. Incident root caries events were defined as decay or restorations on teeth that were previously sound and recurrent events as restorations plus decay on previously restored teeth. Root caries events recorded between each pair of examinations were adjusted for reversals. | analyses of root caries increment. | | | | |
| 2 | UK cohort Rugg-Gunn et al. (1984) Rugg-Gunn et al. (1987) United Kingdom 2 year Public funding | N = 466 Population sampled: Children in their final 2 years of middle school from the area of south Northumberland Excluded: left the area or were absent for part of the study, | Caries increment (continuous variable) of the following indices: DMFT DFS: all surfaces DFS (FS): pit and fissure | 5 times 3-day food diaries (3 consecutive days) in the 2 years of the study (total of 15 days of dietary intake). All days of the week covered. Children were instructed to record all foods and beverages consumed, the | Amount (g/day) (mean±SD) 118 ± 29.4 ~ 21 E% Frequency (times/day) 6.8 ± 1.8 | Caries increment (C3) over 2 years: (mean, 95% range) DMFT: 2.20 (0–7) DFS: 3.63 (0–12) | Model 1: crude Model 2: age, sex, gingival index, frequency of sugars intake, starch intake | DMFS units increment (95%CI) for each 30 g/day of intake Model 2: 0.36 (–0.07, 0.80) Correlation coefficient (P value) |

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person-years | Outcome measure | Model covariates | Results |
|----------|--|---|--|---|--------------------------------|---|------------------|---|
| | | <p>children asked to leave the study, unreliable dietary diaries. n = 405</p> <p>Sex: 52.35% females Ethnicity: Caucasian</p> <p>Age: 11.6 ± 0.3 year</p> | <p>DFS (SS): free smooth DFS (AP): approximal</p> <p>Dental examination at baseline, 1 and 2 years by the same examiner plus radiographs. Visual caries-examining system used to record one pre-cavitation grade (C1) and one cavitation grade (C3). The radiographic grading X1 (enamel only) corresponded to C1 and X2 (at enamel-dentine junction) corresponded to C3. A bilateral recording system was used in</p> | <p>amounts and the time of the day in which these were consumed. Interview the day of completion to check quantities and uncertainties. Food models and graduated cups used for quantification of the amount.</p> <p>Reliability of the measurement of total dietary sugars found to be 0.78⁶⁷</p> | | <p>DFS (FS): 2.10 (-1, 7) DFS (SS): 0.24 (0, 2) DFS (AP): 1.34 (0, 6)</p> <p>Percentage of total carious surfaces</p> <p>DFS (FS): 57 DFS (SS): 7 DFS (AP): 36</p> | | <p>Model 1: DMFT: 0.077 (NS) DFS (FS): 0.105 (P < 0.05) DFS (FS): 0.143 (P < 0.01) DFS (SS): -0.01 (NS) DFS (AP): 0.042 (NS)</p> <p>Model 2: DMFT: NR DFS (FS): 0.082 (NS) DFS (FS): 0.142 (P < 0.01) DFS (SS): 0.023 (NS) DFS (AP): -0.010 (NS)</p> |

⁶⁷ Hackett A. F., Rugg-Gunn A. J. and Appleton D. R. (1983) The use of a dietary diary and interview to estimate the food intake of children. Hum. Nutr. Appl. Nutr. 37A, 293–300.

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person-years | Outcome measure | Model covariates | Results |
|----------|--|---|---|---|--|---|---|--|
| | | | which 71% of teeth were assessed. The reliability of the measurement of dental caries was not assessed; 'previously found to be 0.85 for similar data' ⁶⁸ | | | | | |
| 1 | <p>Michigan cohort</p> <p>Burt et al. (1988) Burt and Szpunar (1994) Szpunar et al. (1995)</p> <p>USA</p> <p>3 years</p> <p>Non-fluoridated area</p> <p>Funding source NR</p> | <p>N = 747</p> <p>Population sampled: General population from three towns with non-fluoridated water supply</p> <p>Excluded: completed less than 3 dietary interviews, were not present for baseline and/or final dental examinations</p> <p>Follow-up rate: 66.8%</p> <p>n = 499</p> | <p>Caries increment (dichotomous; none/some) of the following indices:</p> <p>DMFS: all surfaces</p> <p>DMFS (AP): approximal</p> <p>DMFS (FS): pit and fissure</p> <p>Teeth were dried before examination, transillumination used and caries</p> | <p>3 times 2 24-h diet recalls (as dietary interviews) administered for the previous day. Included weekdays and weekends and covered seasonal variations during the study period. Models provided to assess quantities</p> <p>Intake data from all the interviews for the same child over the 3-year follow-up was averaged.</p> | <p>Amount (E%) (mean ± SD) 26.7 ± 5.0</p> <p>Mean Q1: 23.5 Q4: 29.5</p> <p>n Q1: 125 Q4: 125</p> <p>Amount (g/day) (mean ± SD) 142.90 ± 43.42</p> <p>Mean Q1: 108.9 Q4: 175.0</p> | <p>Number of subjects with 0 caries increment / > 0 caries increment</p> <p>DMFS: 119/310 DMFS (AP): 336/93 DMFS (FS): 130/299</p> <p>Number of subjects with > 0 caries increment (%)</p> <p>DMFS: Q1: 76 (61.3)</p> | <p>Model 1: age and baseline DMFS</p> <p>Mode 2: sex, age, history of previous residence in a fluoridated community, use of fluoride tablets, frequency of topical fluorides, toothbrushing frequency, antibiotic use, parental</p> | <p>Model 1 RR (95%CI) Q4 vs. Q1 (E%) DMFS: 1.22 (1.04, 1.46) DMFS (AP): 1.80 (1.06, 3.10) DMFS (FS): 1.19 (0.99, 1.43)</p> <p>Model 2 Correlation coefficient (P value)</p> <p>Amount (E%) DMFS: 0.062 (P < 0.01) DMFS (AP): 0.055 (P < 0.03) DMFS (FS): 0.044 (P < 0.05)</p> |

⁶⁸ Rugg-Gunn AJ, 1972b. Reliability and Partial Recording in Caries Incremental Studies, pp. 84–93. PhD. thesis, Manchester University, Manchester.

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person-years | Outcome measure | Model covariates | Results |
|----------|--|---|---|---|---|--|---------------------------------|---|
| | | <p>Sex: 47.9% females</p> <p>Age: 10–15 year</p> | <p>diagnosed only when a break in surface enamel was evident. Examiners saw the same children at both examinations (baseline and end of the study), and radiographs were not exposed for ethical reasons. Because these examiners had standardised their diagnoses and had worked together on many studies, their data were pooled, and their inter-examiner replicate examinations were conducted.</p> | | <p>Frequency (times/day) (mean ± SD)</p> <p>4.3 ± 0.6</p> | <p>Q4: 94 (75.2) DMFS (AP): Q1: 17 (13.7) Q4: 31 (24.8) DMFS (FS): Q1: 74 (59.2) Q4: 89 (71.2) Caries increment (continuous) over 3 years (mean ± SD)</p> <p>DMFS: 4.30 ± 3.47 DMFS (AP): 2.44 ± 2.33 DMFS (FS): 3.64 ± 2.71</p> | <p>education, family income</p> | <p>Amount (g/day) DMFS: 0.007 (P < 0.02) DMFS (AP): 0.003 (P = 0.26) DMFS (FS): 0.004 (P = 0.15) Frequency (times/day) DMFS: 0.108 (P = 0.53) DMFS (AP): 0.093 (P = 0.63) DMFS (FS): -0.042 (P = 0.80)</p> |

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person-years | Outcome measure | Model covariates | Results |
|----------|---|---|---|--|--|---|--|---|
| 2 | <p>IFS*</p> <p>Chankanka et al. (2011)</p> <p>USA</p> <p>4 years</p> <p>Public funding</p> | <p>N = 608</p> <p>Population sampled: General population</p> <p>Excluded: less than 2 food diaries between 5 and 8 years of age, missing covariates</p> <p>n = 198</p> <p>Sex: 55% females</p> <p>Ethnicity: 94% Caucasian, 6% Other</p> <p>Age: 5-9 year</p> | <p>Caries increment (continuous variable) over 4 years (surfaces with transition from missing or sound to non-cavitated caries, cavitated caries or fillings).</p> <p>Clinical examinations for dental caries were conducted at 5 (primary dentition) and 9 (mixed dentition) years of age by the same trained and calibrated examiners. Examiners did not differentiate cavitated enamel (D2/d2) and dentine lesions (D3-4/d3-4), thus those lesions were</p> | <p>3-day food diaries (2 weekdays, 1 weekend day) were obtained every 1.5–6 months during the study period. Intakes were averaged for each child to reflect sugar intakes from 5 to 8 years of age.</p> | <p>Amount (g/day) (mean ± SD; range)</p> <p>114.5 ± 27.3; 53.2, 216.0</p> <p>n = 192 in analyses</p> | <p>Caries increment (continuous) over 4 years (mean ± SD)</p> <p>1.63 ± 2.35</p> | <p>Model: Age at medical exam for mixed dentition (follow-up), time interval between exams for primary (baseline) and mixed dentition, sex, surfaces with non-cavitated or cavitated caries or filling at age 5 years, brushing frequency, water fluoride concentration</p> | <p>Any surfaces with new non-cavitated or cavitated caries or filling (age 5–9)</p> <p>Per each 10 g/day increase, OR (95%CI)</p> <p>0.93 (0.83, 1.04)</p> <p>Surfaces with new non-cavitated or cavitated caries or filling (counts, age 5–9)</p> <p>Per each 10 g/day increase, OR (95%CI)</p> <p>0.97 (0.91, 1.04)</p> |

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person-years | Outcome measure | Model covariates | Results |
|--------------------------------|--|---|--|---|---|-----------------|---|---|
| | | | categorised together as D2-3/d2-3. | | | | | |
| Exposure: total sucrose | | | | | | | | |
| 2 | STRIP-1 Ruottinen et al. (2004) Finland 9 years Funding source NR Fluoride concentration in drinking water = 0.3 ppm | N = 1,066 Population sampled: Children attending well-baby clinics of the city of Turku, where the fluoride concentration in drinking water is 0.3 ppm Excluded: refusal to participate in the dental caries examination at 10 year, type 1 diabetes or other diseases that may affect sucrose intake (unspecified) Selected: children in the 5th highest and lowest percentile of sucrose intake n = 66 G1: 33 G2: 33 Sex: 31% females Ethnicity: Caucasian | d₃mft, d₃mft+D₃MFT and D₃MFT scores Dental visit at 10 years of age by the same expert, blinded to the exposure. Caries recorded at the level of cavitation and expressed as d ₃ mft+/D ₃ MFT scores according to WHO (1997). Recordings from visual inspection were completed with radiographic findings (two intra-oral radiographs taken and evaluated by two independent experts in a | 3-day food records (at 13 months) and 4-day food records (thereafter every 6 months until 7 years of age, every 2 years thereafter in the intervention group and every year in the control group until 10 years of age. Records included one weekend day and were reviewed by nutritionist at next visit. Sucrose intake frequency was assessed at 10 years (cross-sectional analysis only, data not extracted) | E% <u>Age 13 mo</u> G1: 2.92 ± 1.73 G2: 7 ± 2.9 <u>Age 10 year</u> G1: 7.29 ± 3.39 G2: 11.92 ± 2.76 g/day <u>Age 13 mo</u> G1: 7.1 ± 4.7 G2: 16.6 ± 7.4 <u>Age 10 year</u> G1: 32.5 ± 18.4 G2: 52.6 ± 13.1 | - | None Authors state that the association between sugar intake and caries was tight in all tooth-brushing frequency groups (sub-group analysis), but failed to reach significance because of the small number of children in each group | d₃mft G1: 1.1 ± 1.2 G2: 2.7 ± 3.3 P = 0.177 d₃mft+D₃MFT G1: 0.5 ± 1.1 G2: 1.9 ± 2.5 P = 0.032 D₃MFT G1: 1.4 ± 2.0 G2: 3.9 ± 3.9 P = 0.01 |

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person-years | Outcome measure | Model covariates | Results |
|----------|--|---|--|---|--|---|--|---|
| 2 | <p>STRIP-2*</p> <p>Karjalainen et al. (2001)</p> <p>Karjalainen et al. (2015)</p> <p>Finland</p> <p>13 years</p> <p>Funding source NR</p> <p>Fluoride concentration in drinking water = 0.3 ppm</p> | <p>Age: 13 months</p> <p>N = 1,066</p> <p>Population sampled: Children attending well-baby clinics of the city of Turku, where the fluoride concentration in drinking water is 0.3 ppm</p> <p>Every fifth child was invited (n = 178) to the dental health study at 3 years of age and attended</p> <p>n = 142</p> <p>Follow-up rate at 16 year: 55.6%</p> <p>Sex: 45.8% females</p> <p>Ethnicity: Caucasian</p> <p>Age: 3 years</p> | <p>random order and blinded to the exposure)</p> <p>d₃mft/D₃MFT scores</p> <p>Dental visits at 3, 6, 9, 12 and 16 years of age by the same expert, blinded to the exposure. Caries recorded at the level of cavitation and expressed as d₃mft+/D₃MFT scores according to WHO (1997).</p> <p>At 16 years, recordings from visual inspection were completed with radiographic findings (two intra-oral radiographs taken and evaluated by two independent experts in a random order</p> | <p>4-day food records at 3, 6, 9, 12 and 16 years of age.</p> <p>Records included one weekend day and were reviewed by nutritionist at next visit.</p> | <p>g/day (median, range)</p> <p>3 years</p> <p>Q1 (ref): 15.9 (7.4, 20.9)</p> <p>Q2: 23.1 (21.0, 25.4)</p> <p>Q3: 29.6 (25.6, 34.4)</p> <p>Q4: 44.0 (34.5, 65.9)</p> <p>n = 128 in analyses</p> <p>12 years</p> <p>Q1 (ref): 19.4 (7.1, 25.7)</p> <p>Q2: 29.4 (26.4, 33.9)</p> <p>Q3: 38.36 (34.3, 42.5.4)</p> <p>Q4: 56.0 (43.7, 78.8)</p> <p>n = 81 in analyses</p> | <p>d₃mft increment (3–6 years) (mean ± SD)</p> <p>0.82 ± 1.89</p> <p>D₃MFT increment (12–16 years) (mean ± SD)</p> <p>2.14 ± 2.47</p> <p>Proportion of counts > 0 (mean ± SD)</p> <p>Any new d₃mft (3–6 years)</p> <p>0.23 ± 0.42</p> <p>Any new D₃MFT (12–16 years)</p> <p>0.68 ± 0.47</p> | <p>Model: sex, STRIP study group, caries-free age and daily toothbrushing</p> | <p>d₃mft increment between 3 and at 6 years (yes/no)</p> <p>Per each 10 g/day increase</p> <p>1.64 (1.13, 2.37)</p> <p>OR (95%CI)</p> <p>Q1 (ref): 1</p> <p>Q2: 1.03 (0.26, 4.01)</p> <p>Q3: 0.91 (0.63, 3.54)</p> <p>Q4: 4.32 (1.31, 14.25)</p> <p>d₃mft increment between 3 and at 6 years (counts)</p> <p>Per each 10 g/day increase</p> <p>1.21 (0.91, 1.61)</p> <p>OR (95%CI)</p> <p>Q1 (ref): 1</p> <p>Q2: 0.59 (0.17, 2.05)</p> <p>Q3: 0.66 (0.23, 1.91)</p> <p>Q4: 1.54 (0.61, 3.89)</p> <p>D₃MFT increment between 12 and at 16 years (yes/no)</p> |

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person-years | Outcome measure | Model covariates | Results |
|-----------------------|--|---|---|--|---|--|---|---|
| | | | and blinded to the exposure) | | | | | <p>Per each 10 g/day increase 0.95 (0.68, 1.34) OR (95%CI) Q1 (ref): 1 Q2: 1.16 (0.30, 4.50) Q3: 3.16 (0.63, 15.75) Q4: 0.70 (0.17, 2.84)</p> <p>D₃MFT increment between 12 and at 16 years (counts)</p> <p>Per each 10 g/day increase 0.99 (0.84, 1.18) OR (95%CI) Q1 (ref): 1 Q2: 1.35 (0.66, 1.78) Q3: 1.29 (0.69, 2.42) Q4: 1.09 (0.53, 2.22)</p> |
| Exposure: SSSD | | | | | | | | |
| 2 | <p>VA-DLS Kaye et al. (2015)* USA mean 11 ± 5 years, range 2.5–19.6 years Public funding?</p> | <p>Same population and exclusion criteria as for total sugars</p> | <p>Same ascertainment of outcome as for total sugars</p> | <p>Same exposure assessment as for total sugars</p> | <p>Servings/wk (median, range) Q1: 0, 0–0.09 Q2: 0.34, 0.11–0.84 Q3: 1.52, 0.85–2.35 Q4: 4.20, 2.36–24.8</p> | <p>Same as for total sugars</p> | <p>Model: years at risk of root caries and baseline values of age, smoking status, number of teeth at risk for root caries, existing root caries/restorations,</p> | <p>Adjusted Root Caries Increment, mean (95%CI) Q1: 2.17 (1.68–2.79) Q2: 2.64 (2.06–3.37) Q3: 2.57 (2.01–3.29) Q4: 2.86 (2.28–3.60) P per trend < 0.05</p> |

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person-years | Outcome measure | Model covariates | Results |
|----------------------|---|---|--|---|--|---------------------------------|---|--|
| | | | | | Serving size = 12 oz (335 mL) n Q1: 118 Q2: 148 Q3: 133 Q4: 134 | | subgingival calculus on one or more surfaces, prophylaxis in past year and removable denture | |
| 2 | IFS (Chankanka et al., 2011) USA Public funding | Same population and exclusion criteria as for total sugars | Same ascertainment of outcome as for total sugars | Same exposure assessment as for total sugars | Amount (mL/day) (mean ± SD; range) 272 ± 175; 0, 1,079 | Same as for total sugars | Model: Age at medical exam for mixed dentition (follow-up), time interval between exams for primary (baseline) and mixed dentition, sex, surfaces with non-cavitated or cavitated caries or filling at age 5 years, brushing frequency, water fluoride concentration | Any surfaces with new non-cavitated or cavitated caries or filling (age 5–9) Per each 100 mL/day increase, OR (95%CI) 1.01 (0.85, 1.21) Surfaces with new non-cavitated or cavitated caries or filling (counts, age 5–9) Per each 100 mL/day increase, OR (95%CI) 1.01 (0.88, 1.17) |
| Exposure: FJs | | | | | | | | |
| 2 | IFS Chankanka et al. (2011) | Same population and exclusion criteria as for total sugars | Same ascertainment of outcome as | Same exposure assessment as for total sugars | Amount (mL/day) (mean ± SD; range) | Same as for total sugars | Model: Age at medical exam for mixed dentition (follow- | Any surfaces with new non-cavitated or cavitated caries or filling (age 5–9) |

| RoB Tier | Cohort References Country Follow-up Funding | Population (recruited) Exclusion criteria Study population (n, sex and age at baseline) | Outcome Ascertainment of outcome | Exposure assessment, time coverage and validation | Exposure groups n/person-years | Outcome measure | Model covariates | Results |
|----------|--|---|----------------------------------|---|--------------------------------|-----------------|---|---|
| | USA Public funding | | for total sugars | | 87 ± 79; 0, 525 | | up), time interval between exams for primary (baseline) and mixed dentition, sex, surfaces with non-cavitated or cavitated caries or filling at age 5 years, brushing frequency, water fluoride concentration | Per each 100 mL/day increase, OR (95%CI) 0.83 (0.55, 1.26) Surfaces with new non-cavitated or cavitated caries or filling (counts, age 5–9) Per each 100 mL/day increase, OR (95%CI) 0.96 (0.75, 1.24) |

D3MFT, decayed into dentine, missing and filled permanent teeth; d3mft, decayed into dentine, missing and filled primary teeth; DFS: decayed, filled surfaces; DFS (AP), approximal surfaces; DFS (FS), pit and fissure surfaces; DFS (SS), free smooth surfaces; DMFS: decayed, missing and filled surfaces; DMFT: decayed, missing and filled permanent teeth; dmft: decayed, missing and filled primary teeth; FFQ, food frequency questionnaire; FJ, fruit juice; SFFQ, semiquantitative food frequency questionnaire; SSSD, sugar-sweetened soft drinks.

*: Individual data provided by the authors.

** : Information provided by the authors.

List of Annexes

These Annexes can be found in the online version of this output, under the section 'Supporting information', at: <https://doi.org/10.2903/j.efsa.2022.7074>

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Annex K – Outcome of the appraisal of human studies in relation to the risk of bias

Annex L – Statistical analysis of intervention studies on metabolic diseases

Annex M – Statistical analysis of observational studies on metabolic diseases

Annex N – Statistical analysis of observational studies on dental caries

Annex O – Technical report: outcome of the public consultation on the draft Scientific opinion on the Tolerable Upper Intake Level for dietary sugars