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

HRs from MOST ADJ models sorted by increasing exposure

									HR per category /				
Publication	Study	Age.	N	N	Exposure	Exposure	Exposure, Median	Sex	HR per unit		Hazard		
(Author, Year)	Location	range	participants	events/cases	category code	unit STD	and/or Range	code	change (ref/unit)		Ratio (95% CI)	Note	TEI
MDCS CVD incidence													
Sonestedt et al., 2015	Sweden	44 - 74	164894*	1342	SSSD	mL/day	0.0	Mixed	NC (ref)	*	1.00 (1.00, 1.00)		STD
Sonestedt et al., 2015	Sweden	44 - 74	67500*	490	SSSD	mL/day	26.0	Mixed	Q1	•+	0.93 (0.84, 1.03)		STD
Sonestedt et al., 2015	Sweden	44 - 74	67072*	532	SSSD	mL/day	89.0	Mixed	Q2	+*	1.06 (0.96, 1.18)		STD
Sonestedt et al., 2015	Sweden	44 - 74	65467*	557	SSSD	mL/day	306.0	Mixed	Q3	+-	1.00 (0.90, 1.11)		STD
CTS CVD incidence													
Pacheco et al., 2020	USA	22 - 84	43425	4648	SSSD+SSFD	mL/day	0.0	Females	NC (ref)	*	1.00 (1.00, 1.00)		
Pacheco et al., 2020	USA	22 - 84	35422	2382	SSSD+SSFD	mL/day	77.0	Females	C1	+	1.01 (0.96, 1.07)		
Pacheco et al., 2020	USA	22 - 84	22825	1494	SSSD+SSFD	mL/day	163.0	Females	C2	+	1.02 (0.96, 1.09)		
Pacheco et al., 2020	USA	22 - 84	4506	324	SSSD+SSFD	mL/day	400.0	Females	C3		1.19 (1.06, 1.34)		
EPIC-Multicentre CVD	mortality												
Mullee et al., 2019	DK, DE, GR, FR, NL, UK, NO	35 - 70	181131	3311	SSSD+SSFD	mL/day	1.0 (< .25)	Mixed	Q1 (ref)	*	1.00 (1.00, 1.00)		
Mullee et al., 2019	DK, DE, GR, FR, NL, UK, NO	35 - 70	40376	955	SSSD+SSFD	mL/day	20.9 (.25 - 1)	Mixed	Q2		0.97 (0.90, 1.05)		
Mullee et al., 2019	DK, DE, GR, FR, NL, UK, NO	35 - 70	64178	1206	SSSD+SSFD	mL/day	98.0 (1 - 6)	Mixed	Q3 .	*	0.96 (0.89, 1.03)		
Mullee et al., 2019	DK, DE, GR, FR, NL, UK, NO	35 - 70	9371	220	SSSD+SSFD	mL/day	308.4 (7 - 14)	Mixed	Q4		1.06 (0.92, 1.22)		
Mullee et al., 2019	DK, DE, GR, FR, NL, UK, NO	35 - 70	6746	175	SSSD+SSFD	mL/day	708.8 (> 14)	Mixed	Q5	++-	1.11 (0.95, 1.30)		
NHS CVD mortality													
Malik et al., 2019	USA	30 - 55	1127585*	1883	SSSD+SSFD	mL/day	< 13	Females	Q1 (ref)	+	1.00 (1.00, 1.00)		
Malik et al., 2019	USA	30 - 55	604268*	972	SSSD+SSFD	mL/day	13 - 51	Females	Q2	++-	1.07 (0.99, 1.16)		
Malik et al., 2019	USA	30 - 55	522058*	829	SSSD+SSFD	mL/day	101 - 304	Females	Q3	-	1.10 (1.01, 1.20)		
Malik et al., 2019	USA	30 - 55	163412*	293	SSSD+SSFD	mL/day	355 - 710	Females	Q4		1.21 (1.06, 1.38)		
Malik et al., 2019	USA	30 - 55	84884*	162	SSSD+SSFD	mL/day	> 710	Females	Q5		1.37 (1.16, 1.62)		
HPFS CVD mortality													
Malik et al., 2019	USA	40 - 75	348582*	1593	SSSD+SSFD	mL/day	< 13	Males	Q1 (ref)	+	1.00 (1.00, 1.00)		
Malik et al., 2019	USA	40 - 75	168005*	736	SSSD+SSFD	mL/day	13 - 51	Males	Q2		1.04 (0.95, 1.14)		
Malik et al., 2019	USA	40 - 75	302337*	1122	SSSD+SSFD	mL/day	101 - 304	Males	Q3	-	1.08 (0.99, 1.17)		
Malik et al., 2019	USA	40 - 75	66398*	222	SSSD+SSFD	mL/day	355 - 710	Males	Q4		1.17 (1.01, 1.35)		
Malik et al., 2019	USA	40 - 75	28035*	84	SSSD+SSFD	mL/day	> 710	Males	Q5	+	1.19 (0.95, 1.49)		
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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

Publication	Study	Age,	Ν	Ν	Exposure	Exposure	Exposure, Median	Sex		Hazard	%		
(Author, Year)	Location	range	participants	events/cases	category code	unit STD	and/or Range	code		Ratio (95% CI)	Weight	Note	TEI
MDCS CVD incidence													
Sonestedt et al., 2015	Sweden	44 - 74	65467*	557	SSSD	mL/day	306.0	Mixed -	* (1.00 (0.90, 1.11)	25.10		STD
CTS CVD incidence													
Pacheco et al., 2020	USA	22 - 84	4506	324	SSSD+SSFD	mL/day	400.0	Females	-	1.19 (1.06, 1.34)	23.36		
EPIC-Multicentre CVD	mortality												
Mullee et al., 2019	DK, DE, GR, FR, NL, UK, NO	35 - 70	6746	175	SSSD+SSFD	mL/day	708.8 (> 14)	Mixed	<u>+</u>	1.11 (0.95, 1.30)	19.37		
NHS CVD mortality													
Malik et al., 2019	USA	30 - 55	84884*	162	SSSD+SSFD	mL/day	> 710	Females	-	1.37 (1.16, 1.62)	18.42		
HPFS CVD mortality													
Malik et al., 2019	USA	40 - 75	28035*	84	SSSD+SSFD	mL/day	> 710	Males	x	1.19 (0.95, 1.49)	13.75		
Overall (I-squared = 6	6.1%, p = 0.019)								\diamond	1.15 (1.03, 1.29)	100.00		
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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

Publication (Author, Year)	Study	Age, range	N participants	N events/cases	Exposure category code	Exposure unit STD	Exposure, Median and/or Range	Sex code	HR per category / HR per unit change (ref/unit)		Hazard Ratio (95% CI)	Note	TEI
					• /				• • • •				
JPHC CHD incidence										1			
Eshak et al., 2012	Japan	40 - 59	11820	53	SSSD+SSFD+SSFJ	mL/day	0	Females	NC (ref)		1.00 (1.00, 1.00)	OR	
Eshak et al., 2012	Japan	40 - 59	6401	25	SSSD+SSFD+SSFJ	mL/day	36 - 71	Females	Q1 -		0.96 (0.59, 1.56)	OR	
Eshak et al., 2012	Japan	40 - 59	1769	11	SSSD+SSFD+SSFJ	mL/day	107 - 143	Females	Q2	*	1.52 (0.78, 2.96)	OR	
Eshak et al., 2012	Japan	40 - 59	921	4	SSSD+SSFD+SSFJ	mL/day	179 - 250	Females	Q3		0.88 (0.30, 2.59)	OR	
Eshak et al., 2012	Japan	40 - 59	7453	155	SSSD+SSFD+SSFJ	mL/day	0	Males	NC (ref)	*	1.00 (1.00, 1.00)	OR	
Eshak et al., 2012	Japan	40 - 59	6535	112	SSSD+SSFD+SSFJ	mL/day	36 - 71	Males	Q1		0.85 (0.66, 1.09)	OR	
Eshak et al., 2012	Japan	40 - 59	3000	49	SSSD+SSFD+SSFJ	mL/day	107 - 143	Males	Q2 -		0.85 (0.61, 1.18)	OR	
Eshak et al., 2012	Japan	40 - 59	1886	44	SSSD+SSFD+SSFJ	mL/day	179 - 250	Males	Q3		1.04 (0.74, 1.47)	OR	
MDCS CHD incidence										1			
Sonestedt et al., 2015	Sweden	44 - 74	164894*	NR	SSSD	mL/day	0.0	Mixed	NC (ref)	*	1.00 (1.00, 1.00)		STD
Sonestedt et al., 2015	Sweden	44 - 74	67500*	NR	SSSD	mL/day	26.0	Mixed	Q1	- t -	0.98 (0.85, 1.12)		STD
Sonestedt et al., 2015	Sweden	44 - 74	67072*	NR	SSSD	mL/day	89.0	Mixed	Q2		1.05 (0.92, 1.20)		STD
Sonestedt et al., 2015	Sweden	44 - 74	65467*	NR	SSSD	mL/day	306.0	Mixed	Q3	+	1.02 (0.89, 1.16)		STD
CTS CHD incidence										1			
Pacheco et al., 2020	USA	22 - 84	43425	1441	SSSD+SSFD	mL/day	0.0	Females	NC (ref)	.	1.00 (1.00, 1.00)		
Pacheco et al., 2020	USA	22 - 84	35422	681	SSSD+SSFD	mL/day	77.0	Females	C1	+	0.98 (0.89, 1.07)		
Pacheco et al., 2020	USA	22 - 84	22825	460	SSSD+SSFD	mL/day	163.0	Females	C2	-	1.07 (0.96, 1.19)		
Pacheco et al., 2020	USA	22 - 84	4506	95	SSSD+SSFD	mL/day	400.0	Females	C3		1.18 (0.95, 1.47)		
EPIC-Multicentre CHD	mortality									1			
Mullee et al., 2019	DK, DE, GR, FR, NL, UK, NO	35 - 70	178971	1151	SSSD+SSFD	mL/day	1.0 (< .25)	Mixed	Q1 (ref)	*	1.00 (1.00, 1.00)		
Mullee et al., 2019	DK, DE, GR, FR, NL, UK, NO	35 - 70	39798	377	SSSD+SSFD	mL/day	20.9 (.25 - 1)	Mixed	Q2	-	1.03 (0.91, 1.16)		
Mullee et al., 2019	DK, DE, GR, FR, NL, UK, NO	35 - 70	63426	454	SSSD+SSFD	mL/day	98.0 (1 - 6)	Mixed	Q3		0.95 (0.85, 1.07)		
Mullee et al., 2019	DK, DE, GR, FR, NL, UK, NO	35 - 70	15881	159	SSSD+SSFD	mL/day	477.9 (> 7)	Mixed	Q4		1.04 (0.87, 1.24)		
HPP CHD incidence													
Keller et al., 2020	USA	35	274754	4248	SSSD+SSFD	mL/day		Mixed	Per 355 ml/d increase	I. .	1.08 (1.03, 1.14)		
Keller et al., 2020	USA	35	261169	NR	SSSD+SSFD	mL/day	0 - 355	Mixed	Q1 (ref)	Ť	1.00 (1.00, 1.00)		
Keller et al., 2020	USA	35	13463	NR	SSSD+SSFD	mL/day	355 - 710	Mixed	Q2	-	1.12 (0.97, 1.29)		
Keller et al., 2020	USA	35	8791	NR	SSSD+SSFD	mL/day	< 710	Mixed	Q3	+	1.14 (0.93, 1.40)		
REGARDS CHD morta	lity									1			
Collin et al., 2019	USA	45	NR	39	SSSD+SSFD	E%	0-5	Mixed	C1 (ref)	Ī	1.00 (1.00, 1.00)		
Collin et al., 2019	USA	45	NR	29	SSSD+SSFD	E%	5 - 10	Mixed	C2		1.08 (0.70, 1.67)		
Collin et al., 2019	USA	45	NR	100	SSSD+SSFD	E%	> 10	Mixed	C3	-	1.59 (1.06, 2.39)		
Collin et al., 2019	USA	45	13440	168	555D+55FD	mL/day	50.5 (6 - 232.2)	Mixed	Per 355 mi/d increase		1.11 (0.89, 1.38)		
									.5	1 2			

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

Publication	Study	Age,	Ν	Ν	Exposure	Exposure	Exposure, Median	Sex		Hazard	%		
(Author, Year)	Location	range	participants	events/cases	category code	unit STD	and/or Range	code		Ratio (95% CI)	Weight	Note	TEI
JPHC CHD incidenc	e								1				
Eshak et al., 2012	Japan	40 - 59	921	4	SSSD+SSFD+SSF	J mL/day	179 - 250	Females	*	0.88 (0.30, 2.59)	0.57	OR	
Eshak et al., 2012	Japan	40 - 59	1886	44	SSSD+SSFD+SSF.	J mL/day	179 - 250	Males	•••	1.04 (0.74, 1.47)	5.54	OR	
MDCS CHD incident	ce												
Sonestedt et al., 201	5 Sweden	44 - 74	65467*	NR	SSSD	mL/day	306.0	Mixed	—	1.02 (0.89, 1.16)	37.88		STD
									L.				
CTS CHD incidence									:				
Pacheco et al., 2020	USA	22 - 84	4506	95	SSSD+SSFD	mL/day	400.0	Females		1.18 (0.95, 1.47)	13.95		
EPIC-Multicentre CH	ID mortality												
Mullee et al., 2019	DK, DE, GR, FR, NL, UK, N	O35 - 70	15881	159	SSSD+SSFD	mL/day	477.9 (> 7)	Mixed	—	1.04 (0.87, 1.24)	22.18		
									li li				
HPP CHD incidence									li				
Keller et al., 2020	USA	35	8791	NR	SSSD+SSFD	mL/day	< 710	Mixed		1.14 (0.93, 1.40)	15.89		
REGARDS CHD mo	rtality												
Collin et al., 2019	USA	45	NR	100	SSSD+SSFD	E%	> 10	Mixed	· · · · ·	1.59 (1.06, 2.39)	3.98		
Overall (I-squared =	0.0%, p = 0.491)								\diamond	1.08 (1.00, 1.18)	100.00		
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								.5	1 2				

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

Publication (Author, Year)	Study Location	Age, range	N participants	N events/cases	Exposure category code	Exposure unit STD	Exposure, Median and/or Range	Sex code	HR per category / HR per unit change (ref/unit)			Hazard Ratio (95% CI)	Note	TEI
Framingham-Offspring Pase et al., 2017 Pase et al., 2017 Pase et al., 2017	g Stroke incidence USA USA USA	45 45 45	NR NR NR	NR NR NR	SSSD+SSFD SSSD+SSFD SSSD+SSFD	mL/day mL/day mL/day	0 51 - 154 > 154	Mixed Mixed Mixed	NC (ref) C1 C2	*	*	1.00 (1.00, 1.00) 1.14 (0.70, 1.85) 0.80 (0.38, 1.68)		
JPHC Stroke incidenc Eshak et al., 2012 Eshak et al., 2012	ba Japan Japan Japan Japan Japan Japan Japan	40 - 59 40 - 59	11820 6401 1769 921 7453 6535 3000 1886	431 242 74 42 513 385 151 84	SSSD+SSFD+SSFJ SSD+SSFD+SSFJ SSSD+SSFD+SSFJ SSSD+SSFD+SSFJ SSSD+SSFD+SSFJ SSSD+SSFD+SSFJ SSSD+SSFD+SSFJ SSSD+SSFD+SSFJ	mL/day mL/day mL/day mL/day mL/day mL/day mL/day	0 36 - 71 107 - 143 179 - 250 0 36 - 71 107 - 143 179 - 250	Females Females Females Males Males Males Males	NC (ref) Q1 Q2 Q3 NC (ref) Q1 Q2 Q3			1.00 (1.00, 1.00) 1.07 (0.91, 1.25) 1.12 (0.87, 1.44) 1.21 (0.88, 1.67) 1.00 (1.00, 1.00) 0.89 (0.77, 1.03) 0.90 (0.76, 1.06) 0.76 (0.58, 0.99)	OR OR OR OR OR OR OR	
MDCS I-Stroke incide Sonestedt et al., 2015 Sonestedt et al., 2015 Sonestedt et al., 2015 Sonestedt et al., 2015	nce 5 Sweden 5 Sweden 5 Sweden 5 Sweden	44 - 74 44 - 74 44 - 74 44 - 74	164894* 67500* 67072* 65467*	NR NR NR NR	SSSD SSSD SSSD SSSD	mL/day mL/day mL/day mL/day	0.0 260 890 306.0	Mixed Mixed Mixed Mixed	NC (ref) Q1 Q2 Q3		<u>.</u>	1.00 (1.00, 1.00) 0.87 (0.74, 1.02) 1.06 (0.91, 1.24) 0.97 (0.83, 1.13)		STD STD STD STD
HPFS Stroke incidenc Bernstein et al., 2012 Bernstein et al., 2012 Bernstein et al., 2012 Bernstein et al., 2012	xe USA USA USA USA	40 - 75 40 - 75 40 - 75 40 - 75	259630* 204418* 323569* 54153*	464 381 499 72	SSSD SSSD SSSD SSSD	mL/day mL/day mL/day mL/day	0 0 - 51 51 - 355 > 355	Males Males Males Males	NC (ref) Q1 Q2 Q3		-	1.00 (1.00, 1.00) 0.93 (0.80, 1.08) 0.99 (0.86, 1.14) 1.05 (0.80, 1.38)	RR RR RR RR	
NHS Stroke incidence Bernstein et al., 2012 Bernstein et al., 2012 Bernstein et al., 2012 Bernstein et al., 2012	USA USA USA USA	30 - 55 30 - 55 30 - 55 30 - 55	717209* 632223* 693974* 144825*	918 950 896 174	SSSD SSSD SSSD SSSD	mL/day mL/day mL/day mL/day	0 0 - 51 51 - 355 > 355	Females Females Females Females	NC (ref) Q1 Q2 Q3	-	-	1.00 (1.00, 1.00) 1.00 (0.90, 1.11) 1.09 (0.99, 1.21) 1.14 (0.95, 1.36)	RR RR RR RR	
CTS Stroke incidence Pacheco et al., 2020 Pacheco et al., 2020 Pacheco et al., 2020 Pacheco et al., 2020	USA USA USA USA	22 - 84 22 - 84 22 - 84 22 - 84	43425 35422 22825 4506	2787 1415 867 189	SSSD+SSFD SSSD+SSFD SSSD+SSFD SSSD+SSFD	mL/day mL/day mL/day mL/day	0.0 77.0 163.0 400.0	Females Females Females Females	NC (ref) C1 C2 C3	- 11		1.00 (1.00, 1.00) 1.01 (0.95, 1.08) 1.01 (0.93, 1.09) 1.21 (1.04, 1.41)		
EPIC-Multicentre Stro Mullee et al., 2019 Mullee et al., 2019 Mullee et al., 2019 Mullee et al., 2019 Mullee et al., 2019	ke mortality DK, DE, GR, FR, NL, UK, NO DK, DE, GR, FR, NL, UK, NO DK, DE, GR, FR, NL, UK, NO DK, DE, GR, FR, NL, UK, NO	35 - 70 35 - 70 35 - 70 35 - 70 35 - 70	178742 39684 63299 15831	922 263 327 109	SSSD+SSFD SSSD+SSFD SSSD+SSFD SSSD+SSFD	mL/day mL/day mL/day mL/day	1.0 209 980 477.9	Mixed Mixed Mixed Mixed	C1 (ref) C2 C3 C4	-11-		1.00 (1.00, 1.00) 0.97 (0.84, 1.12) 0.99 (0.86, 1.13) 1.19 (0.97, 1.46)		
										.5	1 2			

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

Framingham-Offspring Stroke incidence Pase et al., 2017 USA 45 NR NR SSSD+SSFD mL/day > 154 Mixed 0.80 (0.38, 1.68) 2.04 JPHC Stroke incidence Eshak et al., 2012 Japan 40 - 59 921 42 SSSD+SSFD ML/day 179 - 250 Females 1.21 (0.88, 1.67) 8.29 OR Eshak et al., 2012 Japan 40 - 59 921 42 SSSD+SSFD mL/day 179 - 250 Males 0.76 (0.58, 0.99) 10.69 OR MDCS I-Stroke incidence Sonestedt et al., 2015 Sweden 44 - 74 65467* NR SSSD mL/day 306.0 Mixed 0.97 (0.83, 1.13) 18.70 STD HPFS Stroke incidence Bernstein et al., 2012 USA 40 - 75 54153* 72 SSSD mL/day > 355 Males 1.05 (0.80, 1.38) 10.47 RR NHS Stroke incidence Bernstein et al., 2012 USA 30 - 55 144825* 174 SSSD mL/day > 355 Females 1.14 (0.95, 1.36) 16.55 RR CTS Stroke incidence EpercMulticentre Stroke mortality Mulee et al., 2019 USA <	Publication (Author, Year)	Study Location	Age, range	N participants	N events/cases	Exposure category code	Exposure unit STD	Exposure, Median and/or Range	Sex code		Hazard Ratio (95% CI)	% Weight	Note	TEI
Pase et al., 2017 USA 45 NR NR SSD+SSFD mL/day > 154 Mixed 0.80 (0.38, 1.68) 2.04 <td>Framingham-Offsprin</td> <td>g Stroke incidence</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>1</td> <td></td> <td></td> <td></td> <td></td>	Framingham-Offsprin	g Stroke incidence								1				
JPHC Stroke incidence Eshak et al., 2012 Japan 40 - 59 921 42 SSSD+SSFD *SSFJ 179 - 250 Females 1.21 (0.48, 1.67) 8.29 OR Eshak et al., 2012 Japan 40 - 59 1886 84 SSSD+SSFD+SSFJ mL/day 179 - 250 Males 0.76 (0.58, 0.99) 10.69 OR MCS 1-Stroke incidence MSS 1-SS forke incidence 0.97 (0.83, 1.13) 18.70 STD Sonestedt et al., 2012 USA 40 - 75 54153* 72 SSD mL/day 306.0 Mixed 0.97 (0.83, 1.13) 18.70 STD HPFS Stroke incidence Bernstein et al., 2012 USA 40 - 75 54153* 72 SSD mL/day >355 Males 1.05 (0.80, 1.38) 10.47 RR NHS Stroke incidence Bernstein et al., 2012 USA 30 - 55 14825* 174 SSSD mL/day >355 Females 1.14 (0.95, 1.36) 16.55 RR CTS Stroke incidence Bernstein et al., 2012 USA 22 - 84 4506 189 SSSD+SSFD mL/d	Pase et al., 2017	USA	45	NR	NR	SSSD+SSFD	mL/day	> 154	Mixed 🗲 🔳		0.80 (0.38, 1.68)	2.04		
JPHC Stroke incidence Eshak et al., 2012 Japan 40 - 59 921 42 SSSD+SSFD+SSFJ mL/day 179 - 250 Females 1.21 (0.88, 1.67) 8.29 OR Eshak et al., 2012 Japan 40 - 59 921 42 SSSD+SSFD+SSFJ mL/day 179 - 250 Males 0.76 (0.58, 0.99) 0.89 0R	•													
Eshak et al., 2012 Japan 40 - 59 921 42 SSSD+SSFD mL/day 179 - 250 Females 1.21 (0.88, 1.67) 8.29 OR Eshak et al., 2012 Japan 40 - 59 1886 84 SSSD+SSFD mL/day 179 - 250 Males 0.76 (0.58, 0.99) 0.89 OR MDCS I-Stroke incidence SssDersstedt et al., 2015 Sweden 44 - 74 65467* NR SSSD mL/day 306.0 Mixed 0.97 (0.83, 1.13) 18.70 STD . HPFS Stroke incidence Bernstein et al., 2012 USA 40 - 75 54153* 72 SSSD mL/day >355 Males 1.05 (0.80, 1.38) 10.47 RR 	JPHC Stroke incident	ce												
Eshak et al., 2012 Japan 40 - 59 1886 84 SSSD+SSFJ mL/day 179 - 250 Males 0.76 (0.58, 0.99) 10.69 OR Males 0.76 (0.58, 0.99) 10.69 OR Males <t< td=""><td>Eshak et al., 2012</td><td>Japan</td><td>40 - 59</td><td>921</td><td>42</td><td>SSSD+SSFD+SSFJ</td><td>mL/day</td><td>179 - 250</td><td>Females</td><td></td><td>1.21 (0.88, 1.67)</td><td>8.29</td><td>OR</td><td></td></t<>	Eshak et al., 2012	Japan	40 - 59	921	42	SSSD+SSFD+SSFJ	mL/day	179 - 250	Females		1.21 (0.88, 1.67)	8.29	OR	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Eshak et al., 2012	Japan	40 - 59	1886	84	SSSD+SSFD+SSFJ	mL/day	179 - 250	Males +	-	0.76 (0.58, 0.99)	10.69	OR	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $														
Sonestedt et al., 2015 Sweden 44 - 74 65467* NR SSD mL/day 306.0 Mixed Mixed 0.97 (0.83, 1.13) 18.70 STD . HPFS Stroke incidence Bernstein et al., 2012 USA 40 - 75 54153* 72 SSD mL/day > 355 Males 1.05 (0.80, 1.38) 10.47 RR . NHS Stroke incidence Bernstein et al., 2012 USA 30 - 55 144825* 174 SSD mL/day > 355 Females 1.14 (0.95, 1.36) 16.55 RR .	MDCS I-Stroke incide	ence							_	Li -				
HPFS Stroke incidence Bernstein et al., 2012 USA $40 - 75 54153^{*}$ 72 SSSD mL/day > 355 Males 1.05 (0.80, 1.38) 10.47 RR NHS Stroke incidence Bernstein et al., 2012 USA $30 - 55 144825^{*}$ 174 SSSD mL/day > 355 Females 1.14 (0.95, 1.36) 16.55 RR CTS Stroke incidence Pacheco et al., 2020 USA $22 - 84 4506$ 189 SSSD+SSFD mL/day 400.0 Females 1.21 (1.04, 1.41) 18.89 EPIC-Multicentre Stroke mortality Mulee et al., 2019 DK, DE, GR, FR, NL, UK, NO 35 - 70 15831 109 SSSD+SSFD mL/day 477.9 Mixed 1.19 (0.97, 1.46) 14.36 	Sonestedt et al., 201	5 Sweden	44 - 74	65467*	NR	SSSD	mL/day	306.0	Mixed -	+ <u>+</u>	0.97 (0.83, 1.13)	18.70		STD
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NHS Stroke incidence Bernstein et al., 2012 USA 30 - 55 144825* 174 SSSD mL/day > 355 Females 1.14 (0.95, 1.36) 16.55 RR CTS Stroke incidence Pacheco et al., 2020 USA 22 - 84 4506 189 SSSD+SSFD mL/day 400.0 Females 1.21 (1.04, 1.41) 18.89 .	Bernstein et al., 2012	USA	40 - 75	54153*	72	SSSD	mL/day	> 355	Males	•	1.05 (0.80, 1.38)	10.47	RR	
NHS Stroke incidence Bernstein et al., 2012 USA 30 - 55 144825* 174 SSSD mL/day > 355 Females 1.14 (0.95, 1.36) 16.55 RR CTS Stroke incidence Pacheco et al., 2020 USA 22 - 84 4506 189 SSSD+SSFD mL/day 400.0 Females 1.21 (1.04, 1.41) 18.89 .										II.				
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CTS Stroke incidence Pacheco et al., 2020 USA 22 - 84 4506 189 SSSD+SSFD mL/day 400.0 Females 1.21 (1.04, 1.41) 18.89 . EPIC-Multicentre Stroke mortality Mulee et al., 2019 DK, DE, GR, FR, NL, UK, NO 35 - 70 15831 109 SSSD+SSFD mL/day 477.9 Mixed 1.19 (0.97, 1.46) 14.36 1.07 (0.96, 1.19) 100.00										1				
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EPIC-Multicentre Stroke mortality Mullee et al., 2019 DK, DE, GR, FR, NL, UK, NO 35 - 70 15831 109 SSSD+SSFD mL/day 477.9 Mixed . Overall (Isoguared = 45.9%, p = 0.074)	Pacheco et al., 2020	USA	22 - 84	4506	189	SSSD+SSFD	mL/day	400.0	Females	+ • -	1.21 (1.04, 1.41)	18.89		
EPIC-Multicentre Stroke mortality Mullee et al., 2019 DK, DE, GR, FR, NL, UK, NO 35 - 70 15831 109 SSSD+SSFD mL/day 477.9 Mixed . Overall (Isoguared = 45.9%, p = 0.074) . 107 (0.95, 1.19) 100.00														
Mullee et al., 2019 DK, DE, GR, FR, NL, UK, NO 35 - 70 15831 109 SSSD+SSFD mL/day 477.9 Mixed 1.19 (0.97, 1.46) 14.36	EPIC-Multicentre Stro	oke mortality												
Overall (Lequiared = 45.9%, p = 0.074)	Mullee et al., 2019	DK. DE. GR. FR. NL. UK. NO	35 - 70	15831	109	SSSD+SSFD	mL/day	477.9	Mixed	++++	1.19 (0.97, 1.46)	14.36		
Overall (Jeguared = 45.9% p = 0.074)							,							
	Overall (I-squared =	45.9%, p = 0.074)									1.07 (0.96, 1.19)	100.00		
										Ĩ	(0.00, 0.10)			
									1					
									I .5	1 2				

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

Categorical HRs sorted by cohort, model and increasing exposure

Publication (Author, Year)	Study Location	Age, range	Females proportion	Ethnicity	Person-years	N events/cases	Exposure unit STD	Exposure, Median and/or Range	HR per category (ref)		Hazard Ratio (95% CI)	Note
HPFS Model 1 (le: Choi et al., 2008 Choi et al., 2008 Choi et al., 2008 Choi et al., 2008 Choi et al., 2008	ast adj + BM USA USA USA USA USA USA	II + EI) 40 - 75 40 - 75 40 - 75 40 - 75 40 - 75	0 0 0 0 0	Mixed Mixed Mixed Mixed Mixed	87050 87761 87815 88087 87748	186 139 153 137 140	E% E% E% E%	(0 - 6.9) (6.9 - 8.5) (8.6 - 10) (10.1 - 11.8) (11.8)	Q1 (ref) Q2 Q3 Q4 Q5		1.00 (1.00, 1.00) 0.90 (0.72, 1.13) 1.11 (0.88, 1.40) 1.08 (0.85, 1.37) 1.24 (0.97, 1.58)	RR RR RR RR RR
HPFS Model 1 + c Choi et al., 2008 Choi et al., 2008 Choi et al., 2008 Choi et al., 2008 Choi et al., 2008	covars + fat r USA USA USA USA USA USA	model 40 - 75 40 - 75 40 - 75 40 - 75 40 - 75	0 0 0 0	Mixed Mixed Mixed Mixed Mixed	87050 87761 87815 88087 87748	186 139 153 137 140	E% E% E% E%	(0 - 6.9) (6.9 - 8.5) (8.6 - 10) (10.1 - 11.8) (11.8)	Q1 (ref) Q2 Q3 Q4 Q5		1.00 (1.00, 1.00) 0.96 (0.76, 1.21) 1.20 (0.95, 1.52) 1.25 (0.97, 1.62) 1.52 (1.15, 2.01)	RR RR RR RR RR
HPFS Model 1 + c Choi et al., 2008 Choi et al., 2008 Choi et al., 2008 Choi et al., 2008 Choi et al., 2008	covars + othe USA USA USA USA USA USA	er CHO m 40 - 75 40 - 75 40 - 75 40 - 75 40 - 75 40 - 75	bo 0 0 0 0	Mixed Mixed Mixed Mixed Mixed	87050 87761 87815 88087 87748	186 139 153 137 140	E% E% E% E%	(0 - 6.9) (6.9 - 8.5) (8.6 - 10) (10.1 - 11.8) (11.8)	Q1 (ref) Q2 Q3 Q4 Q5		1.00 (1.00, 1.00) 0.98 (0.77, 1.25) 1.29 (1.00, 1.67) 1.41 (1.06, 1.88) 1.81 (1.31, 2.50)	RR RR RR RR RR
NHS Model 1 (lea: Choi et al., 2010 Choi et al., 2010	st adj + BMI USA USA USA USA USA	+ El) 30 - 55 30 - 55 30 - 55 30 - 55 30 - 55 30 - 55	100 100 100 100 100	Mixed Mixed Mixed Mixed Mixed	300229 320963 326022 327559 315365	154 172 149 163 140	E% E% E% E%	(0 - 7.5) (7.51 - 8.97) (8.97 - 10.2) (10.3 - 11.9) (11.9)	Q1 (ref) Q2 Q3 Q4 Q5	-	1.00 (1.00, 1.00) 1.01 (0.81, 1.26) 0.87 (0.69, 1.10) 0.98 (0.78, 1.24) 0.98 (0.76, 1.26)	RR RR RR RR RR
NHS Model 1 + co Choi et al., 2010 Choi et al., 2010 Choi et al., 2010 Choi et al., 2010 Choi et al., 2010	ovars + fat m USA USA USA USA USA USA	odel 30 - 55 30 - 55 30 - 55 30 - 55 30 - 55 30 - 55	100 100 100 100 100	Mixed Mixed Mixed Mixed Mixed	300229 320963 326022 327559 315365	154 172 149 163 140	E% E% E% E%	(0 - 7.5) (7.51 - 8.97) (8.97 - 10.2) (10.3 - 11.9) (11.9)	Q1 (ref) Q2 Q3 Q4 Q5		1.00 (1.00, 1.00) 1.14 (0.91, 1.43) 1.02 (0.80, 1.31) 1.18 (0.91, 1.53) 1.18 (0.89, 1.56)	RR RR RR RR RR
NHS Model 1 + cc Choi et al., 2010 Choi et al., 2010 Choi et al., 2010 Choi et al., 2010 Choi et al., 2010	ovars + other USA USA USA USA USA	CHO mo 30 - 55 30 - 55 30 - 55 30 - 55 30 - 55 30 - 55	d 100 100 100 100 100	Mixed Mixed Mixed Mixed Mixed	300229 320963 326022 327559 315365	154 172 149 163 140	E% E% E% E% E%	(0 - 7.5) (7.51 - 8.97) (8.97 - 10.2) (10.3 - 11.9) (11.9)	Q1 (ref) Q2 Q3 Q4 Q5		1.00 (1.00, 1.00) 1.23 (0.97, 1.56) 1.17 (0.89, 1.53) 1.41 (1.06, 1.88) 1.44 (1.04, 2.00)	RR RR RR RR RR
										I I .5 1 2		

Note: RR= Rate ratio.

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



	Publication (Author, Year)	Study Location	Age, range	Females proportion	Ethnicity	Person-years	N events/cases	Exposure unit STD	Exposure, Median and/or Range	HR per category (ref)			Hazard Ratio (95% CI)	Note
	HPFS Model 1 (lea Choi et al., 2008 Choi et al., 2008 Choi et al., 2008 Choi et al., 2008 Choi et al., 2008	ast adj + BM USA USA USA USA USA	II + EI) 40 - 75 40 - 75 40 - 75 40 - 75 40 - 75 40 - 75	0 0 0 0 0	Mixed Mixed Mixed Mixed Mixed	87136 87618 87818 88050 87839	152 154 146 160 143	E% E% E% E% E%	(0 - 3.5) (3.5 - 4.4) (4.5 - 5.3) (5.4 - 6.6) (6.6)	Q1 (ref) Q2 Q3 Q4 Q5	8	*	1.00 (1.00, 1.00) 1.19 (0.95, 1.49) 1.21 (0.96, 1.53) 1.45 (1.15, 1.83) 1.43 (1.12, 1.83)	RR RR RR RR RR
	HPFS Model 1 + c Choi et al., 2008 Choi et al., 2008 Choi et al., 2008 Choi et al., 2008 Choi et al., 2008	ovars + fat r USA USA USA USA USA	model 40 - 75 40 - 75 40 - 75 40 - 75 40 - 75	0 0 0 0 0	Mixed Mixed Mixed Mixed	87136 87618 87818 88050 87839	152 154 146 160 143	E% E% E% E%	(0 - 3.5) (3.5 - 4.4) (4.5 - 5.3) (5.4 - 6.6) (6.6)	Q1 (ref) Q2 Q3 Q4 Q5			1.00 (1.00, 1.00) 1.26 (1.00, 1.59) 1.33 (1.04, 1.70) 1.68 (1.30, 2.17) 1.81 (1.38, 2.38)	RR RR RR RR RR
	HPFS Model 1 + c Choi et al., 2008 Choi et al., 2008	ovars + othe USA USA USA USA USA	er CHO m 40 - 75 40 - 75 40 - 75 40 - 75 40 - 75	od 0 0 0 0	Mixed Mixed Mixed Mixed Mixed	87136 87618 87818 88050 87839	152 154 146 160 143	E% E% E% E%	(0 - 3.5) (3.5 - 4.4) (4.5 - 5.3) (5.4 - 6.6) (6.6)	Q1 (ref) Q2 Q3 Q4 Q5	•		1.00 (1.00, 1.00) 1.29 (1.02, 1.64) 1.41 (1.09, 1.82) 1.84 (1.40, 2.41) 2.02 (1.49, 2.74)	RR RR RR RR RR
	NHS Model 1 (leas Choi et al., 2010 Choi et al., 2010 Choi et al., 2010 Choi et al., 2010 Choi et al., 2010	st adj + BMI USA USA USA USA USA USA	+ El) 30 - 55 30 - 55 30 - 55 30 - 55 30 - 55	100 100 100 100 100	Mixed Mixed Mixed Mixed Mixed	294841 320317 327349 329706 317937	132 181 150 160 155	E% E% E% E%	(0 - 3.7) (3.71 - 4.6) (4.61 - 5.45) (5.46 - 6.6) (6.6)	Q1 (ref) Q2 Q3 Q4 Q5	-		1.00 (1.00, 1.00) 1.13 (0.90, 1.42) 0.91 (0.72, 1.16) 0.99 (0.78, 1.26) 1.14 (0.90, 1.45)	RR RR RR RR RR
	NHS Model 1 + co Choi et al., 2010 Choi et al., 2010 Choi et al., 2010 Choi et al., 2010 Choi et al., 2010	vars + fat m USA USA USA USA USA	odel 30 - 55 30 - 55 30 - 55 30 - 55 30 - 55	100 100 100 100 100	Mixed Mixed Mixed Mixed Mixed	294841 320317 327349 329706 317937	132 181 150 160 155	E% E% E% E%	(0 - 3.7) (3.71 - 4.6) (4.61 - 5.45) (5.46 - 6.6) (6.6)	Q1 (ref) Q2 Q3 Q4 Q5	-	* *	1.00 (1.00, 1.00) 1.25 (0.99, 1.58) 1.07 (0.83, 1.37) 1.21 (0.93, 1.57) 1.43 (1.09, 1.88)	RR RR RR RR RR
	NHS Model 1 + co Choi et al., 2010 Choi et al., 2010 Choi et al., 2010 Choi et al., 2010 Choi et al., 2010	vars + other USA USA USA USA USA	CHO mo 30 - 55 30 - 55 30 - 55 30 - 55 30 - 55 30 - 55	d 100 100 100 100 100	Mixed Mixed Mixed Mixed Mixed	294841 320317 327349 329706 317937	132 181 150 160 155	E% E% E% E%	(0 - 3.7) (3.71 - 4.6) (4.61 - 5.45) (5.46 - 6.6) (6.6)	Q1 (ref) Q2 Q3 Q4 Q5	-	* *** ***	1.00 (1.00, 1.00) 1.31 (1.03, 1.66) 1.15 (0.89, 1.49) 1.34 (1.02, 1.77) 1.62 (1.20, 2.19)	RR RR RR RR RR
-											.5 1	 2		

Categorical HRs sorted by cohort, model and increasing exposure

Note: RR= Rate ratio.

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

Publication (Author, Year)	Study Location	Age, range	Females proportion	Ethnicity	Person-years	N events/cases	Exposure unit STD	Exposure, Median and/or Range	HR per category (ref)	Hazard Ratio (95% CI)	Note
HPFS Model 1 (le	ast adj + BN	/II + EI)									
Choi et al., 2008	USA	40 - 75	0	Mixed	158891	279	mL/day	(0 - 13)	C1 (ref)	1.00 (1.00, 1.0))) RR
Choi et al., 2008	USA	40 - 75	0	Mixed	151173	251	mL/day	(14 - 51)	C2	1.00 (0.84, 1.1) RR
Choi et al., 2008	USA	40 - 75	0	Mixed	53086	82	mL/day	(101 - 203)	C3	1.00 (0.78, 1.2) RR
Choi et al., 2008	USA	40 - 75	0	Mixed	47433	88	mL/day	(254 - 304)	C4	1.30 (1.01, 1.6	') RR
Choi et al., 2008	USA	40 - 75	0	Mixed	20485	39	mL/day	355.0	C5	1.44 (1.02, 2.0) RR
Choi et al., 2008	USA	40 - 75	0	Mixed	7392	16	mL/day	(710)	C6	1.78 (1.06, 2.9	3) RR
HPFS Model 1 (B	MI + EI) + o	ovars									
Choi et al., 2008	USA	40 - 75	0	Mixed	158891	279	mL/day	(0 - 13)	C1 (ref)	1.00 (1.00, 1.0))) RR
Choi et al., 2008	USA	40 - 75	0	Mixed	151173	251	mL/day	(13 - 51)	C2)) RR
Choi et al., 2008	USA	40 - 75	0	Mixed	53086	82	mL/day	(101 - 203)	C3	0.99 (0.76, 1.2	3) RR
Choi et al., 2008	USA	40 - 75	0	Mixed	47433	88	mL/day	(254 - 304)	C4	1.29 (1.00, 1.6	() RR
Choi et al., 2008	USA	40 - 75	0	Mixed	20485	39	mL/day	355.0	C5	1.45 (1.02, 2.0	') RR
Choi et al., 2008	USA	40 - 75	0	Mixed	7392	16	mL/day	(710)	C6	1.85 (1.08, 3.1	i) RR
NHS Model 1 (lea	st adj + BM	l + El)									
Choi et al., 2010	USA	30 - 55	100	Mixed	789469	383	mL/day	(0 - 13)	C1 (ref)	1.00 (1.00, 1.0) RR
Choi et al., 2010	USA	30 - 55	100	Mixed	387106	187	mL/day	(14 - 51)	C2	1.12 (0.94, 1.3	3) RR
Choi et al., 2010	USA	30 - 55	100	Mixed	282172	129	mL/day	(101 - 203)	C3	1.07 (0.88, 1.3	I) RR
Choi et al., 2010	USA	30 - 55	100	Mixed	66390	35	mL/day	(254 - 304)	C4	1.42 (1.00, 2.0)	2) RR
Choi et al., 2010	USA	30 - 55	100	Mixed	47634	31	mL/day	355.0	C5	2.09 (1.44, 3.0	3) RR
Choi et al., 2010	USA	30 - 55	100	Mixed	17379	13	mL/day	(710)	C6	→ 3.05 (1.74, 5.3	5) RR
NHS Model 1 (BM	1I + EI) + co	vars									
Choi et al., 2010	USA	30 - 55	100	Mixed	789469	383	mL/dav	(0 - 13)	C1 (ref)	1.00 (1.00, 1.0)) RR
Choi et al., 2010	USA	30 - 55	100	Mixed	387106	187	mL/day	(13 - 51)	C2	1.09 (0.91, 1.3)) RR
Choi et al., 2010	USA	30 - 55	100	Mixed	282172	129	mL/day	(101 - 203)	C3	0.98 (0.80, 1.2	I) RR
Choi et al., 2010	USA	30 - 55	100	Mixed	66390	35	mL/day	(254 - 304)	C4	1.25 (0.88, 1.7)	3) RR
Choi et al., 2010	USA	30 - 55	100	Mixed	47634	31	mL/day	355.0	C5	1.74 (1.19, 2.5	5) RR
Choi et al., 2010	USA	30 - 55	100	Mixed	17379	13	mL/day	(710)	C6	2.39 (1.34, 4.2	3) RR
										.5 1 2	

Categorical HRs s	sorted by cohort,	model and	increasing	exposure
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Note: RR= Rate ratio

Figure K.19: SSBs and incidence of gout

Publication (Author, Year)	Study Location	Age, range	Females proportion	Ethnicity	Person-years	N events/cases	Exposure unit STD	Exposure, Median and/or Range	HR per category (ref)		Hazard Ratio (95% CI)	Note
HPFS Model 1 (le	ast adj + BN	/I + EI)										
Choi et al., 2008	USA	40 - 75	0	Mixed	26590	31	mL/day	(0 - 6)	C1 (ref)	+	1.00 (1.00, 1.00)	RR
Choi et al., 2008	USA	40 - 75	0	Mixed	85201	137	mL/day	(7 - 25)	C2		1.37 (0.92, 2.03)	RR
Choi et al., 2008	USA	40 - 75	0	Mixed	61964	116	mL/day	(51 - 101)	C3		1.64 (1.10, 2.45)	RR
Choi et al., 2008	USA	40 - 75	0	Mixed	107415	191	mL/day	(126 - 152)	C4		1.60 (1.09, 2.35)	RR
Choi et al., 2008	USA	40 - 75	0	Mixed	129859	236	mL/day	177.0	C5		1.76 (1.20, 2.58)	RR
Choi et al., 2008	USA	40 - 75	0	Mixed	26144	43	mL/day	(354)	C6		1.83 (1.14, 2.93)	RR
HPFS Model 1 (B	MI + EI) + c	ovars										
Choi et al., 2008	USA	40 - 75	0	Mixed	26590	31	mL/day	(0 - 6)	C1 (ref)	* .	1.00 (1.00, 1.00)	RR
Choi et al., 2008	USA	40 - 75	0	Mixed	85201	137	mL/day	(6 - 25)	C2	++-	1.34 (0.91, 1.98)	RR
Choi et al., 2008	USA	40 - 75	0	Mixed	61964	116	mL/day	(51 - 101)	C3		1.57 (1.05, 2.35)	RR
Choi et al., 2008	USA	40 - 75	0	Mixed	107415	191	mL/day	(126 - 152)	C4		1.55 (1.05, 2.29)	RR
Choi et al., 2008	USA	40 - 75	0	Mixed	129859	236	mL/day	177.0	C5		1.74 (1.18, 2.56)	RR
Choi et al., 2008	USA	40 - 75	0	Mixed	26144	43	mL/day	(354)	C6		1.81 (1.12, 2.93)	RR
		-										
NHS Model 1 (lea	ist adj + BMI	+ EI)	100		040047			(0, 0)	01 (
Choi et al., 2010	USA	30 - 55	100	Mixed	213647	/1	mL/day	(0 - 6)	C1 (ref)	1.	1.00 (1.00, 1.00)	RR
Choi et al., 2010	USA	30 - 55	100	Mixed	346219	145	mL/day	(7 - 25)	62		1.33 (1.00, 1.77)	RR
Choi et al., 2010	USA	30 - 55	100	Mixed	506760	277	mL/day	(51 - 101)	03		1.39 (1.07, 1.81)	RR
Choi et al., 2010	USA	30 - 55	100	Mixed	208032	1/1	mL/day	(120 - 152)	64		1.59 (1.20, 2.10)	RR
Choi et al., 2010	USA	30 - 55	100	Mixed	230894	103	mL/day	177.0	C5	· ·	1.48 (1.09, 2.01)	RR
Choi et al., 2010	USA	30 - 55	100	Mixed	10099		mL/day	(354)	6		2.52 (1.55, 4.77)	KK
NHS Model 1 (BM	1I + EI) + co	vars										
Choi et al., 2010	USA	30 - 55	100	Mixed	213647	71	mL/dav	(0 - 6)	C1 (ref)	+	1.00 (1.00, 1.00)	RR
Choi et al., 2010	USA	30 - 55	100	Mixed	346219	145	mL/day	(6 - 25)	C2	_	1.27 (0.95, 1.69)	RR
Choi et al., 2010	USA	30 - 55	100	Mixed	506760	277	mL/day	(51 - 101)	C3		1.30 (0.99, 1.70)	RR
Choi et al., 2010	USA	30 - 55	100	Mixed	268532	171	mL/day	(126 - 152)	C4		1.50 (1.12, 2.00)	RR
Choi et al., 2010	USA	30 - 55	100	Mixed	236894	103	mL/day	177.0	C5		1.41 (1.03, 1.93)	RR
Choi et al., 2010	USA	30 - 55	100	Mixed	18099	11	mL/day	(354)	C6		2.42 (1.27, 4.62)	RR
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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 an	I measures of body fat and abdominal fat
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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	of abdominal	obesity
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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



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

Table L.4a: SSBs and continuous variables related to the risk of obesity and abdominal ob	besity
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 $WC_{BMI}=WC$ regressed on BMI.

Table L.4b:	SSBs and measures	of bod	y fat and	abdominal	fat
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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).



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

Table L.5: FJs	and continuous	variables	related	to	the	risk	of	obesity
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 $WC_{BMI} = WC$ regressed on BMI.

Table L.6 :	Total sugars and incidence of T2	ЭΜ
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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

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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.9: FJs and incidence of T2DM

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.

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.11 : SSBs and incidence of hypertension

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



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

Table L.13:	Fructose and incidence	and/or mortality	of	cardiovascular	diseases
		and/or moreancy	0.	curaiovasculai	albeabeb

:: 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
Exposu	re: 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) 110.9 ± 47.8; 13.7–442.3 Frequency (times/day) (mean ± SD; range) 3.2 ± 2.4; 0–15.6	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	



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 \pm SD (range)): 2.6 \pm 2.9 (0–23) Teeth with reversals: 1.1 \pm 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
		children asked to leave the study, unreliable dietary diaries. n = 405 Sex: 52.35% females Ethnicity: Caucasian Age: 11.6 \pm 0.3 year	DFS (SS): free smooth DFS (AP): approximal 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 (C1) and one 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	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. Reliability of the measurement of total dietary sugars found to be 0.78 ⁶⁷		DFS (FS): 2.10 (-1, 7) DFS (SS): 0.24 (0, 2) DFS (AP): 1.34 (0, 6) Percentage of total carious surfaces DFS (FS): 57 DFS (SS): 7 DFS (AP): 36		Model 1: DMFT: 0.077 (NS) DFS: 0.105 (P < 0.05) DFS (FS): 0.143 (P < 0.01) DFS (SS): -0.01 (NS) DFS (AP): 0.042 (NS) Model 2: DMFT: NR DFS: 0. 082 (NS) DFS (FS): 0.142 (P < 0.01) DFS (SS): 0.023 (NS) DFS (AP): -0.010 (NS)

⁶⁷ Hackett A. F., Rugg-Gunn A. J. and Appleton D. R. (I 983) The use of a dietary diary and interview to estimate the food intake of children. Hum. Nutr. Appl. Nutr. 37A, 293–300.

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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	Michigan cohort Burt et al. (1988) Burt and Szpunar (1994) Szpunar et al. (1995) USA 3 years Non-fluoridated area Funding source NR	N = 747 Population sampled: General population from three towns with non- fluoridated water supply Excluded: completed less than 3 dietary interviews, were not present for baseline and/or final dental examinations Follow-up rate: 66.8% n = 499	Caries increment (dichotomous; none/some) of the following indices: DMFS: all surfaces DMFS (AP): approximal DMFS (FS): pit and fissure Teeth were dried before examination, transillumination used and caries	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 Intake data from all the interviews for the same child over the 3- year follow-up was averaged.	Amount (E%) (mean \pm SD) 26.7 \pm 5.0 Mean Q1: 23.5 Q4: 29.5 n Q1: 125 Q4: 125 Amount (g/ day) (mean \pm SD) 142.90 \pm 43.42 Mean Q1: 108.9 Q4: 175 0	Number of subjects with 0 caries increment/> 0 caries increment DMFS: 119/310 DMFS (AP): 336/93 DMFS (FS):130/299 Number of subjects with > 0 caries increment (%) DMFS: O1: 76 (61.3)	Model 1: age and baseline DMFS 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	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) Model 2 Correlation coefficient (P value) Amount (E%) DMFS: 0.062 (P < 0.01) DMFS: (AP): 0.055 (P < 0.03) DMFS (FS): 0.044 (P < 0.05)

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

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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
		Sex: 47.9% females Age: 10–15 year	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.		Frequency (times/day) (mean ± SD) 4.3 ± 0.6	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 \pm SD) DMFS: 4.30 \pm 3.47 DMFS (AP): 2.44 \pm 2.33 DMFS (FS): 3.64 \pm 2.71	education, family income	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)



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	IFS* Chankanka et al. (2011) USA 4 years Public funding	N = 608 Population sampled: General population Excluded: less than 2 food diaries between 5 and 8 years of age, missing covariates n = 198 Sex: 55% females Ethnicity: 94% Caucasian, 6% Other Age: 5-9 year	Caries increment (continuous variable) over 4 years (surfaces with transition from missing or sound to non-cavitated caries, cavitated caries or fillings). 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	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.	Amount (g/ day) (mean ± SD; range) 114.5 ± 27.3; 53.2, 216.0 n = 192 in analyses	Caries increment (continuous) over 4 years (mean ± SD) 1.63 ± 2.35	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 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 10 g/day increase, OR (95%CI) 0.93 (0.83, 1.04) Surfaces with new non-cavitated or cavitated caries or filling (counts, age 5–9) Per each 10 g/day increase, OR (95%CI) 0.97 (0.91, 1.04)



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.							
Exposu	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 	d ₃ mft, d ₃ mft+ D ₃ MFT and D ₃ MFT 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 (<i>cross-sectional</i> <i>analysis only, data</i> <i>not extracted</i>)	E% <u>Age 13 mo</u> G1: 2.92 \pm 1.73 G2: 7 \pm 2.9 <u>Age 10 year</u> G1: 7.29 \pm 3.39 G2: 11.92 \pm 2.76 g/day <u>Age 13 mo</u> G1: 7.1 \pm 4.7 G2: 16.6 \pm 7.4 <u>Age 10 year</u> G1: 32.5 \pm 18.4 G2: 52.6 \pm 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			



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
		Age: 13 months	random order and blinded to the exposure)					
2	STRIP-2* Karjalainen et al. (2001) Karjalainen et al. (2015) Finland 13 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 Every fifth child was invited (n = 178) to the dental health study at 3 years of age and attended n = 142 Follow-up rate at 16 year: 55.6% Sex: 45.8% females Ethnicity : Caucasian Age: 3 years	d ₃ mft/D ₃ MFT scores 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 d ₃ mft+/D ₃ MFT scores according to WHO (1997). 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	4-day food records at 3, 6, 9, 12 and 16 years of age. Records included one weekend day and were reviewed by nutritionist at next visit.	g/day (median, range) 3 years Q1 (ref): 15.9 (7.4, 20.9) Q2: 23.1 (21.0, 25.4) Q3: 29.6 (25.6, 34.4) Q4: 44.0 (34.5, 65.9) n = 128 in analyses 12 years Q1 (ref): 19.4 (7.1, 25.7) Q2: 29.4 (26.4, 33.9) Q3: 38.36 (34.3, 42.5.4) Q4: 56.0 (43.7, 78.8) n = 81 in analyses		Model: sex, STRIP study group, caries- free age and daily toothbrushing	$d_{3}mft incrementbetween 3 and at6 years (yes/no)Per each 10 g/dayincrease1.64 (1.13, 2.37)OR (95%CI)Q1 (ref): 1Q2: 1.03 (0.26, 4.01)Q3: 0.91 (0.63, 3.54)Q4: 4.32 (1.31, 14.25)d_3mft incrementbetween 3 and at6 years (counts)Per each 10 g/dayincrease1.21 (0.91, 1.61)OR (95%CI)Q1 (ref): 1Q2: 0.59 (0.17, 2.05)Q3: 0.66 (0.23, 1.91)Q4: 1.54 (0.61, 3.89)D_3MFT incrementbetween 12 and at16 years (yes/no)$



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)					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)
								D ₃ MFT increment between 12 and at 16 years (counts)
								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)
Exposu	re: SSSD							
2	VA-DLS Kaye et al. (2015)*	Same population and exclusion criteria as for total sugars	Same ascertainment of outcome as for total	Same exposure assessment as for total sugars	Servings/wk (median, range) Q1: 0, 0–0.09	Same as for total sugars	Model : years at risk of root caries and baseline values	Adjusted Root Caries Increment, mean (95%CI)
	USA mean 11 ± 5 years, range 2.5–19.6 years Public funding?		sugars		Q2: 0.34, 0.11– 0.84 Q3: 1.52, 0.85– 2.35 Q4: 4.20, 2.36– 24.8		of age, smoking status, number of teeth at risk for root caries, existing root caries/	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
	. ablic randing:						restorations,	



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 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)		
Exposu	xposure: 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		for total		87 ± 79; 0, 525		up), time	Per each 100 mL/day
	Public funding		sugars				interval between exams for primary (baseline) and mixed dentition, sex, surfaces with non- cavitated or cavitated or cavitated caries or filling at age 5 years, brushing frequency, water fluoride concentration	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 J – Evidence tables for observational studies on metabolic diseases

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

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