Vitenskapskomiteen for mat og miljø

Norwegian Scientific Committee for Food and Environment

The risk of caffeine consumption from multiple sources among 8-18 year-olds in Norway

Ellen Bruzell

Nordic symposium: Energy drinks and young people · Rekjavík · October 22 · 2019

A request by the Norwegian Food Safety Authority (NFSA)

VKM, Bruzell E, Hauger Carlsen M, Granum B, Lillegaard IT, Mathisen GH, Rasinger JD, Svendsen C, Devold TG, Rohloff J, Husøy T (2019). VKM report 2019:01, ISBN: 978-82-8259-317-5, ISSN: 2535-4019.

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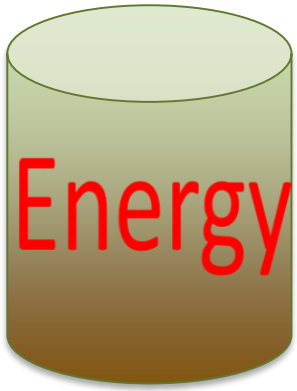
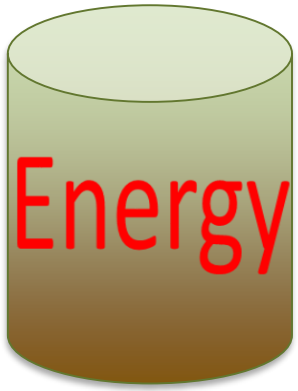
«Definition»* of energy drink

Either

≥ 15 mg caffeine/dl



Or



≥ 15 mg caffeine/dl

+ one or more of:

- **plant substances**
- **amino acids**
- **vitamins**
- **minerals**

- No alcohol
- May contain sugar and/or sweetener

Always caffeine

**From Terms of Reference, NFSA*

Other limitations

- **Children and adolescents: 8-18 years**, not including pregnant and lactating women
- **Norwegian intake** studies and surveys
- Assessment of only the **negative** health effects
- No assessment of health effects of **sugar content and acidity** (e.g. overweight, tooth health)
- Effect studies on **humans** only

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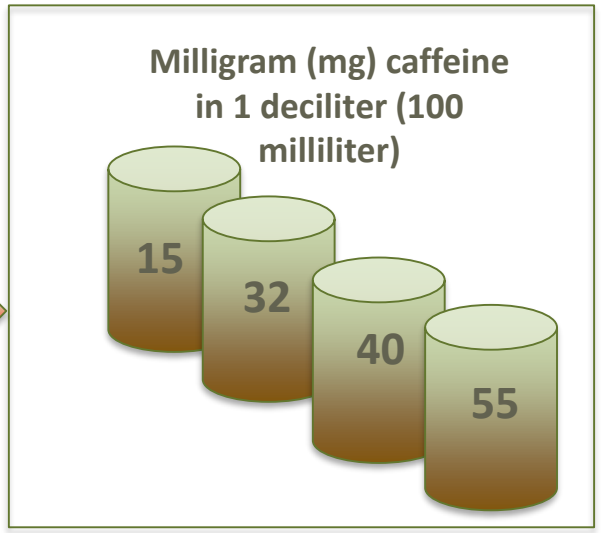
The request

1.

Intake of energy drinks:

- *Highest acute*
- *Median chronic*
- *High chronic*



2.


+


3.


+


Caffeine in food and drinks

4.



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Caffeine content in drinks

- Stimulating, addictive, abstinence upon withdrawal.
- Individual tolerance can be developed.

milligram caffeine per deciliter

Sources: EFSA 2015 (Table 1, pg. 21)
VKM 2019, Appendix 16

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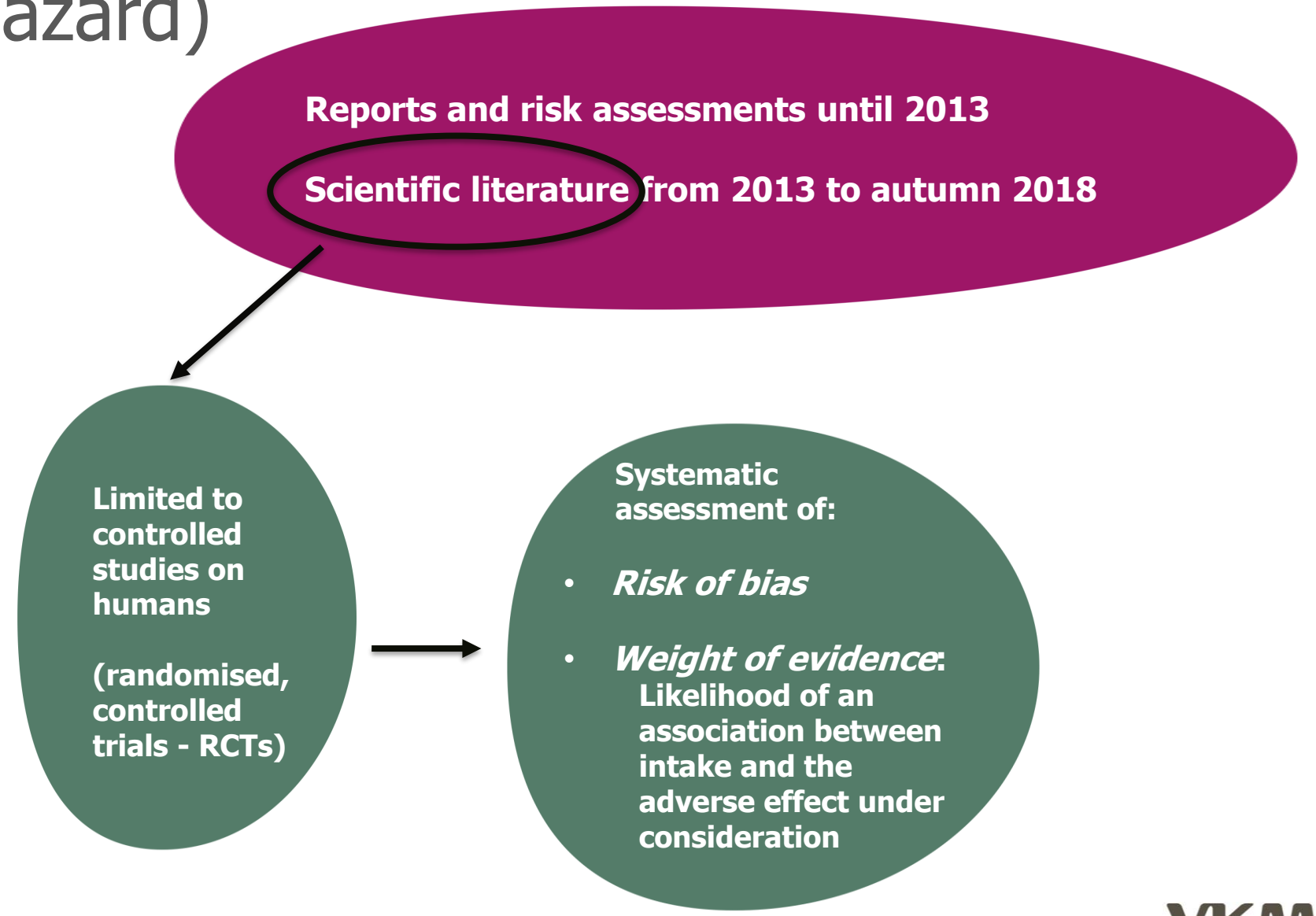
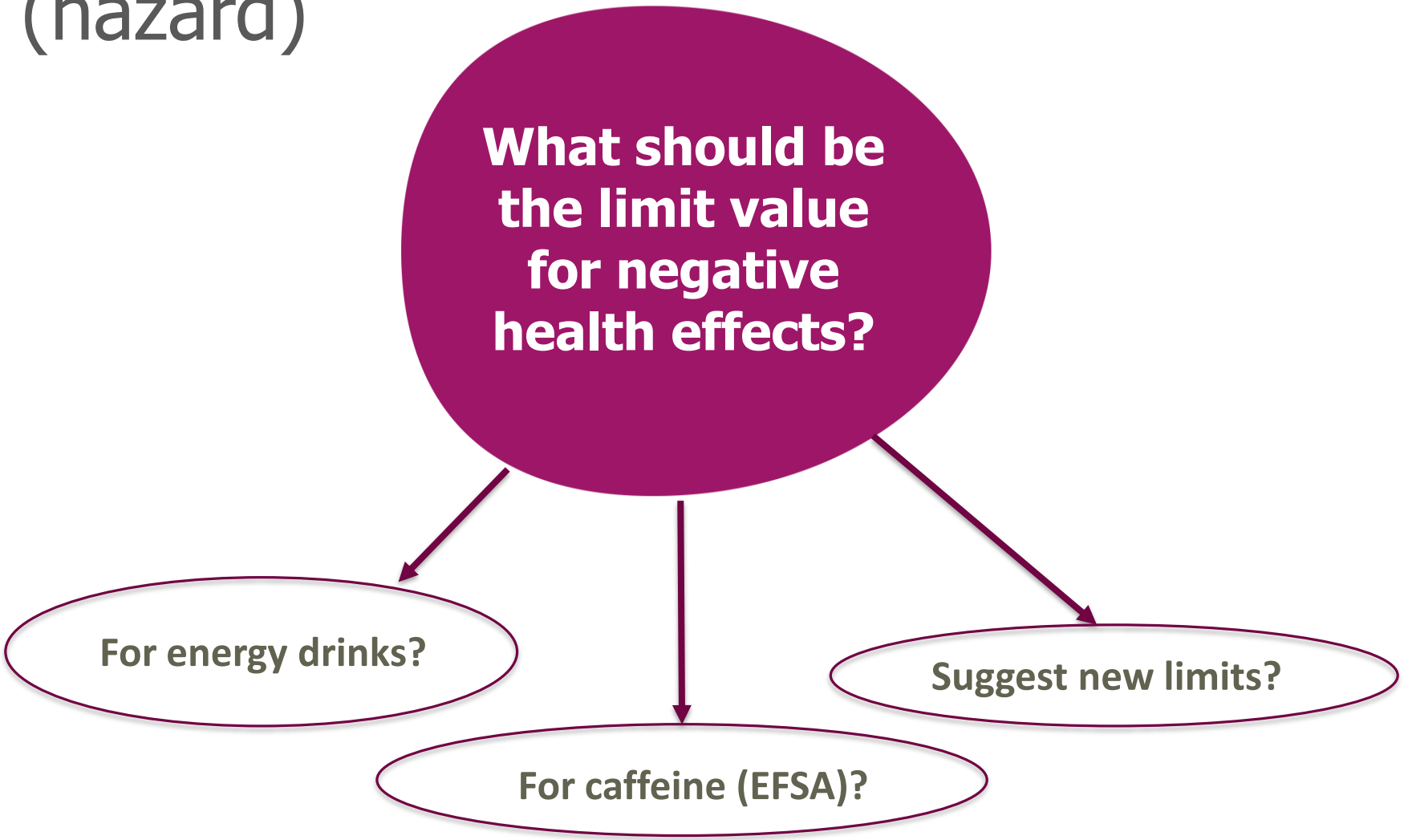
Assessment of negative health effects (hazard)



Assessment of negative health effects (hazard)



EFSA: European Food Safety Authority

Assessment of intake

Energy drink intake?

Total intake of caffeine from the diet?

Study	Data collection (yr)	Participant age (yr)	Participants (#)	Response rate (%)
«Ungkost 3»	2015	8-9; 12-13	1323	54
«Norwegian Consumer Council»	2018	10-12; 13-15; 16-18	962	28
«MoBa»*	2017-2018	13-15	15767	30
«Ungdata»	2016-2018	13-15; 16-18	44894	67

*The Norwegian Mother and Child Cohort Follow-up Study

Results and conclusions: *negative health effects*

No evidence that energy drinks induce other effects

or that the effects are stronger or weaker

than those of caffeine

VKM applies EFSA's limits for safe intake of caffeine

1.4 mg caffeine/kg bodyweight per day:

sleep disturbance

3 mg caffeine/kg bodyweight per day:

«general» negative health effects

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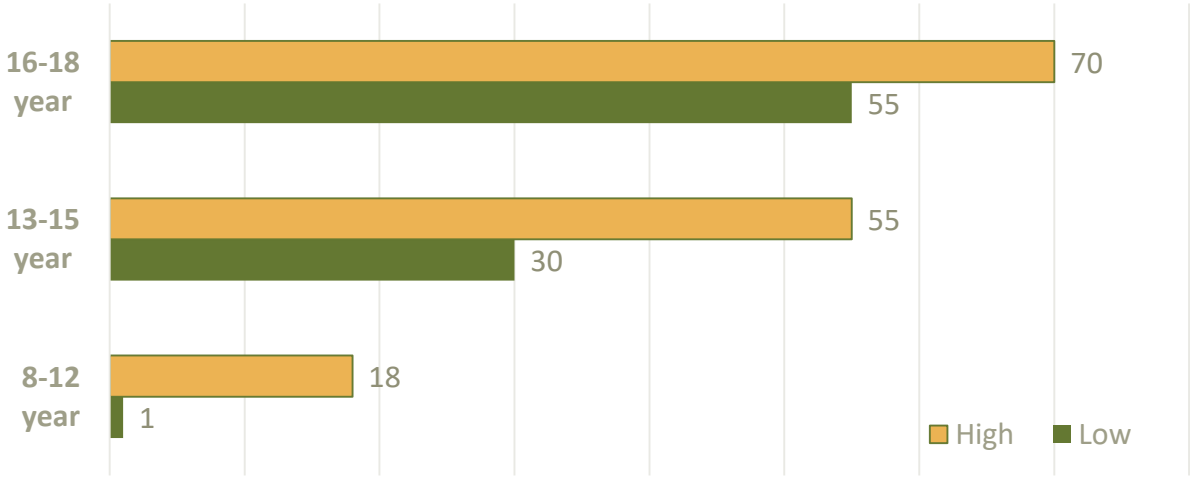
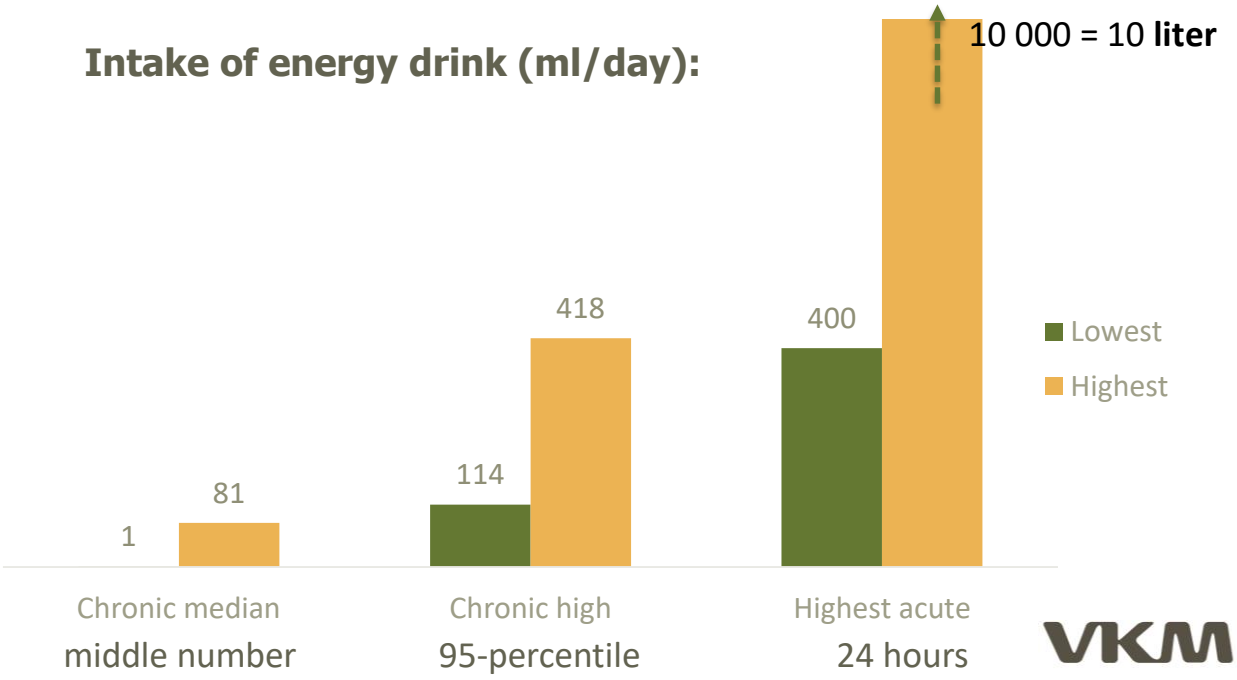
Results and conclusions: *intake*

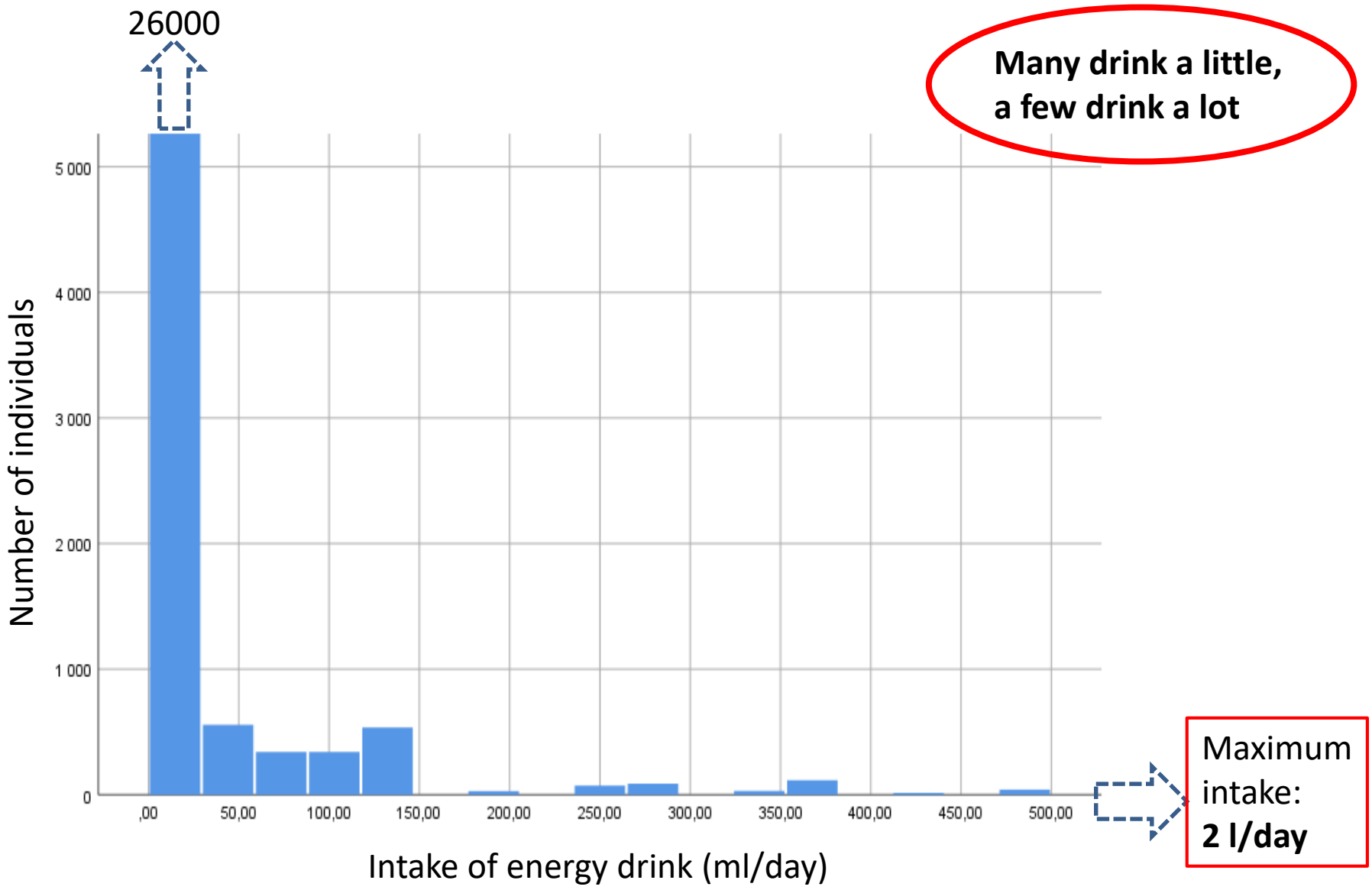
The percentage (%) energy drink conumers, all studies combined

Across studies: 45%





Intake of energy drink among adolescent consumers*of energy drink, skewed data



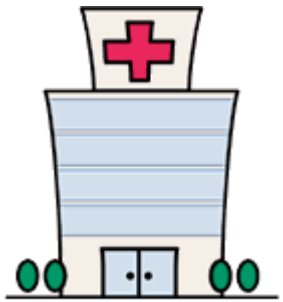
*Source: Ungdata, Oslo Metropolitan University. Figure: Monica Carlsen, University of Oslo/VKM

Keep in mind:

Multiple caffeine sources

Some groups are more susceptible than others to energy drinks and caffeine

8-18 yr old energy drink consumers tend to consume more caffeine from other sources as well



Increased hazard!

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Risk assessment

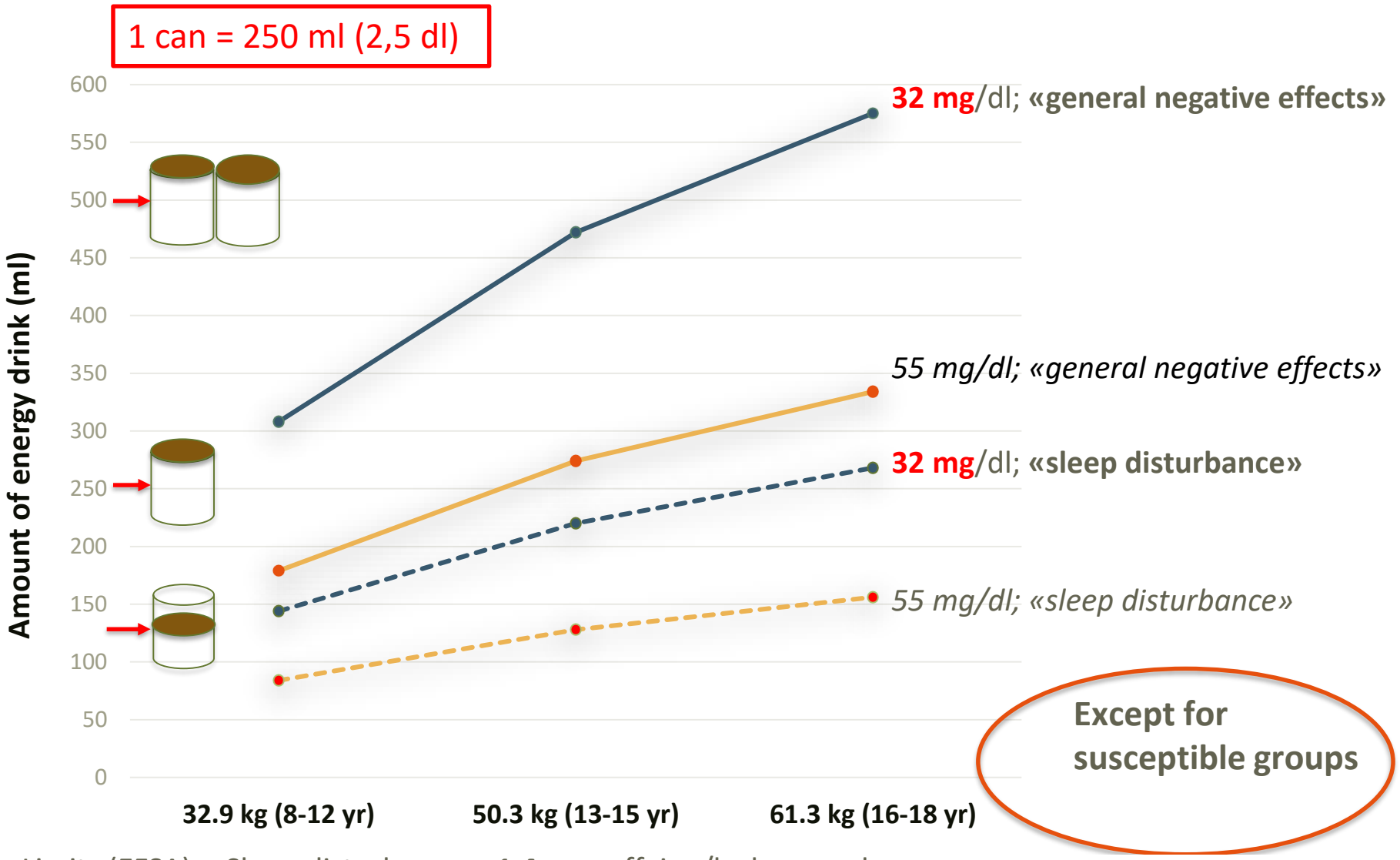
Hazard

Exposure

VS.

What is the risk?

Highest advisable intake of energy drink



Limits (EFSA): «Sleep disturbance»: **1,4 mg** caffeine/kg bw per day

«General negative health effects»: **3 mg** caffeine/kg bw per day

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Energy drink intake risk

Age, yr	Drinking pattern *24 hours	Amount caffeine per 1 dl energy drink			
		15 mg	**32 mg**	**40 mg**	**55 mg**
8-12	Chronic median				
	Chronic high				
	Highest acute*				
13-15	Chronic median				
	Chronic high				
	Highest acute*				
16-18	Chronic median				
	Chronic high				
	Highest acute*				

low or no risk

may pose a risk of sleep disturbances

may pose a risk of general negative health effects

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Caffeine intake risk

*Caffeine in **food and drinks*** except energy drink*

	Non-energy drink consumers		Energy drink consumers	
Age (yr)	Chronic median	Chronic high	Chronic median	Chronic high
8-9				Cannot conclude
12-13				

low or no risk

*Ungkost 3: Food and drinks, not soda beverages. Underestimation

Caffeine intake risk

Caffeine in **drinks*** except energy drink

	Non-energy drink consumers		Energy drink consumers	
Age (yr)	Chronic median	Chronic high	Chronic median	Chronic high
10-12				
13-15				
16-18				

low or no risk

may pose a risk of sleep disturbances

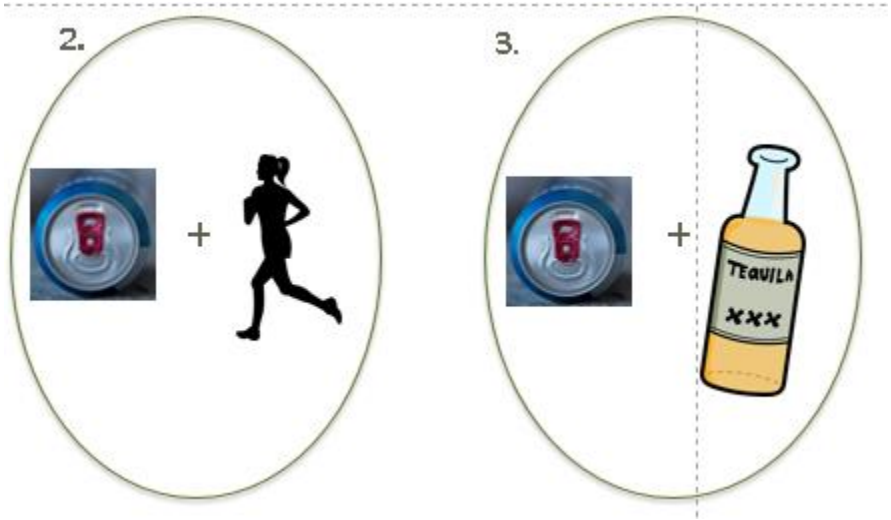
may pose a risk of general negative health effects

*Norwegian Consumer Council-study: only drinks, no food. Underestimation

Energy drink in combination with exercise or alcohol (from RCTs)

- **Exercise/physical activity:** Few data. No adverse health effects *after* the activity (*during* activity was not assessed). Dehydration was not assessed in the RCTs.

- **Alcohol:** Cannot draw any conclusions about central nervous system effects.



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Uncertainties (non-exhaustive list)

- Negative health effects (hazard):
  - Lack of knowledge of the dose-response relationship
  - Relatively low doses of caffeine were given in the RCTs
  - Effects following high doses are not well described
  - Data are mostly based on adult exposure and effects

- Intake
  - Few study participants in some groups
  - Not all sources of caffeine are included
  - Responses are based on memory, may be biased

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Methodolgy: Use of data extraction

Study ID

a. Reference
b. Health outcome(s)

Funding

a. Funding source(s)
b. Reported conflict of interest

Study design

a. Study type (e.g. RCT, cohort, etc.)
b. Type of blinding
c. Method for randomization
d. Year the study was conducted (start/stop)

Subjects

a. Number of participants in the study (invited, accepted, drop out, participating, included in follow-up if applicable)
b. Completion rate
c. Number of exposed/non-exposed subjects or number of cases/controls
d. Sex (male/female)
e. Geography (country)
f. Age
g. Ethnicity
h. Confounders and other variables as reported
i. Health status of participants
j. Inclusion/exclusion criteria
k. Other

Intervention/exposure

a. Test substance
b. Estimated dietary exposure/intake (measures of variance as presented in paper such as mean, standard deviation, median, percentiles, minimum/maximum)
c. Intervention design
d. Co-exposure description (if applicable)

Methods for endpoint assessment

a. Parameters measured and methods used
b. Measurement time points

Statistical analysis

a. Power analysis
b. Statistical test
c. Results and outcome assessment

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RCT quality assessment method: Risk of bias

Example		
Number	Question	Rating (++,+,-,--)
1	Was administered dose or exposure level adequately randomized?	+
2	Were subjects blinded to the study group during the study?	-
3	Were research personnel blinded to the study group during the study?	- NR
4	Were outcome data complete without attrition or exclusion from analysis?	-
5	Can we be confident in the exposure characterization?	+
6	Can we be confident in the outcome assessment (including blinding of outcome assessors)?	- -
7	Were all measured outcomes reported?	- -
8	Where there no other potential threats to internal validity?	+
Conclusion		**TIER 3**

Method Source: Modified from **Office of Health Assessment and Translation** (OHAT) Risk of Bias Tool for Human and Animal Studies, National Toxicology Program, NIH, USA, 2015

Number	Question	Rating (**++,+,-,--**) (not complete, see OHAT-report)
1	*Was administered dose or exposure level adequately randomized?* • Definitely low risk of bias (++) • Probably low risk of bias (+) • Probably high risk of bias/not reported (NR) (–) • Definitely high risk of bias (– –)	++: Direct evidence of allocation to group with randomisation method (includes restricted randomisation e.g. blocked randomisation) +: indirect evidence of random allocation (authors state that allocation was random), no method reported **OR** lack of clear random component would not appreciably bias results -: Indirect evidence of non-random component **OR** insufficient information about subject allocation to study group (record NR) --: Direct evidence of allocation using non-random method (clinician judgement, availability of intervention, etc.)

Division of studies into quality levels

Tier 1:

- All the key questions are scored + /++

AND

- No more than one non-key question is scored –

AND

- No non-key question is scored – –

Tier 2:

- All the other combinations not falling under tier 1 or 3

Tier 3:

- Any key or any non-key question is scored – –

OR

- More than one key question is scored –

Methodology: Weight of evidence

1. Assessed each study per endpoint

Degree of confidence in the association between intervention and effect

- **High confidence (++++)** in the association between exposure to the substance and the outcome. The true effect is highly likely to be reflected in the apparent relationship.
- **Moderate confidence (+++)** in the association between exposure to the substance and the outcome. The true effect may be reflected in the apparent relationship.
- **Low confidence (++)** in the association between exposure to the substance and the outcome. The true effect may be different from the apparent relationship.
- **Very low confidence (+)** in the association between exposure to the substance and the outcome. The true effect is highly likely to be different from the apparent relationship. (Further termed "inadequate" in OHAT Handbook (NTP 2015a)).

Modified from Office of Health Assessment and Translation (OHAT) Risk of Bias Tool for Human and Animal Studies, OHAT, National Toxicology Program, 2015

Weight of Evidence

2. Overall assessment of all studies with the same endpoint

Is there a likely association between intervention and effect?

Table 3.1.4-2. Set of terms used to transform the final rating of confidence in the evidence per endpoint of all relevant randomised controlled trials to overall likelihood.

	Overall confidence of evidence rating range	**Likelihood of an association between intake of energy drinks/exposure to caffeine and the adverse effect under consideration**
Health effect present	++++	Very likely
	From ++++ to +++	Likely
	From +++ to ++	As likely as not
	From ++ to +	Unlikely
	+	Very unlikely/inadequate evidence of health effect
Health effect not present	++++	Evidence of no health effect
	From +++ to +	Inadequate evidence of health effect

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Work sheet for «weight of evidence» assessment

e.g.change in blood pressure after intake of energy drink

Endpoint [describe]:

	Elements triggering downgrading				Elements triggering upgrading				
Study (name)	**Risk of bias (tiers 1-3)**	**Funding/COI bias**	**Unexplained inconsistency**	**Imprecision**	**Large effect**	**Dose-response relationship**	**Residual confounding**	**Consistency (for final rating only)**	**Rating of individual study**
1	3: very serious 2: serious 1: not serious concern	Very serious or not serious concern	Very serious, serious or not serious concern	Very serious, serious or not serious concern	Large or not large	Yes or no	Yes or no	Yes or no	++++ +++ ++ +
2 *[Repeat procedure for relevant studies]*									
All studies (initial rating ≥ +++)	• Describe trend • Describe key questions • Describe issues	• Describe issues	• Describe results in terms of consistency • Explain apparent inconsistency (if it can be explained)	• Discuss ability to distinguish treatment from control • Describe confidence intervals (if relevant)	• Describe magnitude of response	• Outline evidence for or against dose-response	• Presence of effect or association despite the presence of residual confounding, increases confidence in the association	• Describe model or population consistency	**Final rating:** +/++/+++/++++ For health effect: Very likely/likely/as likely as not/ unlikely/very unlikely For no effect: If ++++: very likely If <++++: inadequate level of evidence

++++

++++/+++

+++/++

++/+

+

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- The project group:
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- Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics
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- VKM's secretariat
- Norwegian Food Safety Authority

THANKS!

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Thank you for listening