



Viten skapskomiteen for mat og miljø

Norwegian Scientific Committee for Food and Environment

Use of epidemiological studies in a benefit and risk assessment of fish intake by VKM

Christine L. Parr, PhD

Senior advisor, epidemiology, VKM Secretariat

ChristineLouise.Parr@vkm.no

www.VKM.no



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Vitenskapskomiteen for mat og miljø
Norwegian Scientific Committee for Food and Environment



VKM Report 2022: 17

Benefit and risk assessment of fish in the Norwegian diet

**Scientific Opinion of the Steering Committee of the Norwegian Scientific
Committee for Food and Environment**

<https://www.vkm.no/english>

About VKM

- Part of the national government administration, provides different agencies with risk- or benefit/risk assessments, and other science-based evidence
- Our main commissioners
 - Food Safety Authority
 - Environment Agency
 - (Medicines Agency- if GMO involved)
 - (Directorate of Health)
- Focal point for the European Food Safety Authority (EFSA)



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Background for fish report

- Fish – an important source of nutrients and contaminants
- National dietary guideline for fish intake in Norway questioned after EFSA lowered the tolerable weekly intake (TWIs) of dioxins and dioxin-like PCBs (dl-PCBs) in 2018¹
 - Critical health effect: reduced semen quality
- Perfluorinated alkylated substances (PFASs) in 2020²
 - Critical health effect: reduced vaccine response in children

1. EFSA Panel on Contaminants in the Food Chain (2018): *Risk for animal and human health related to the presence of dioxins and dioxin-like PCBs in feed and food*. EFSA J, 2018. **16**(11): p. e05333.

2. EFSA Panel on Contaminants in the Food Chain (2020): *Risk to human health related to the presence of perfluoroalkyl substances in food*. EFSA J, 2020. **18**(9): p. e06223.

Terms of reference – Norwegian food safety authority

To estimate health consequences for the Norwegian population if fish intake:

- 1) remains at current level
- 2) increases to meet recommendations by the Directorate of Health

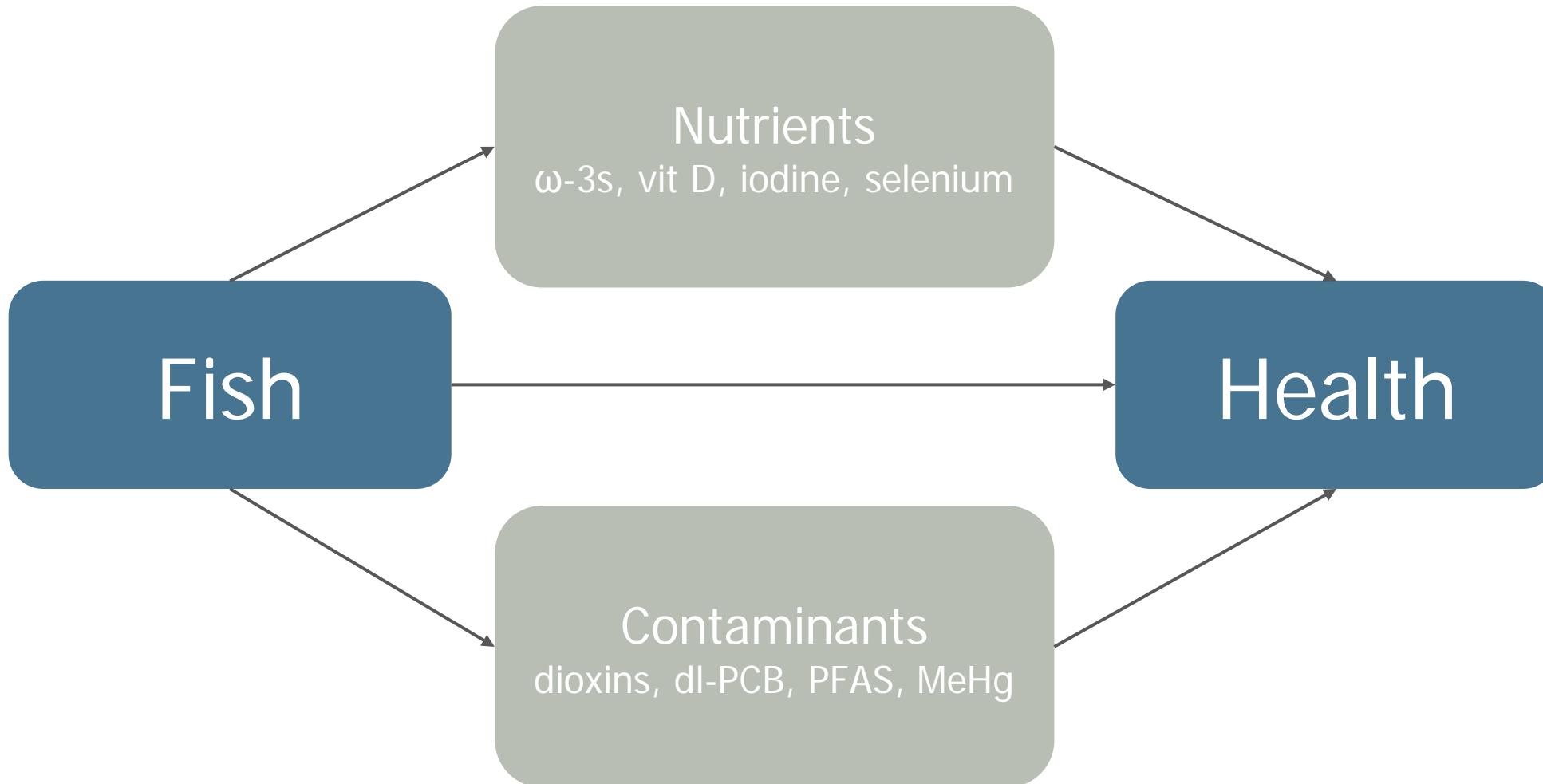
Current recommendation:

- Eat fish for dinner 2-3 times/week, use fish as spread on bread
- Around 300-450 g/week in adults, min 200 g should be fatty fish

VKM have used 3 scenarios:

- 150, 300, and 450 g/week vs. current intake

Fish – integrates nutrients and contaminants



How did we use epidemiological studies?

- In the benefit/risk identification and characterization
- Systematic literature review (SLR) of epi-evidence on health outcomes for
 - Fish intake: primary studies and SLRs; high-low meta-analysis (pooled RR)
 - Nutrients in fish (omega-3 fatty acids, vit D, iodine, selenium): SLRs only
- Contaminants in fish (dioxins, dl-PCB, PFAS, MeHg): epi-evidence evaluated by EFSA when setting tolerable weekly intakes (TWI)
- For outcomes graded «probable» (or higher) for causal effect,
 - Meta dose-response figures from SLRs used for modelling impacts of changes in fish intake on disease incidence or mortality

Health outcomes summarized for fish intake in VKM report

Mortality all-cause, cause specific (adults)	Cardiovascular diseases incidence and mortality (adults)	Cognition, cognitive decline (adults)	Type 2 diabetes (adults)
Hip fractures (adults)	Rheumatoid arthritis (adults)	Multiple sclerosis (adults)	Birth outcomes (preterm birth, SGA, LBW)
Mental disorders, e.g. autism, ADHD (children)	Neurodevelopment (children)	Asthma and allergies (children)	Weight/overweight/ body composition (children, adults)
Cancer (World Cancer Research Fund 2018)	Semen quality and male fertility (empty review)	Vaccine response (empty review)	

Amount of literature on health outcomes

- Primary studies on fish intake (inception to Oct 2021):
 - Around 26 000 screened by title/abstract
 - Around 350 quality assessed
 - 270 included (1%)
- Review studies on fish intake (from 2016 to Oct 2021):
 - Around 800 screened by title/abstract
 - Around 60 quality assessed
 - Around 40 included (5%)
- Review studies on nutrient intakes (ω -3s, vit D, iodine, selenium) from 4 searches:
 - Around 2000 screened by title/abstract
 - Around 80 quality assessed
 - Around 40 included (2%)

Quality assessment/risk of bias (RoB)

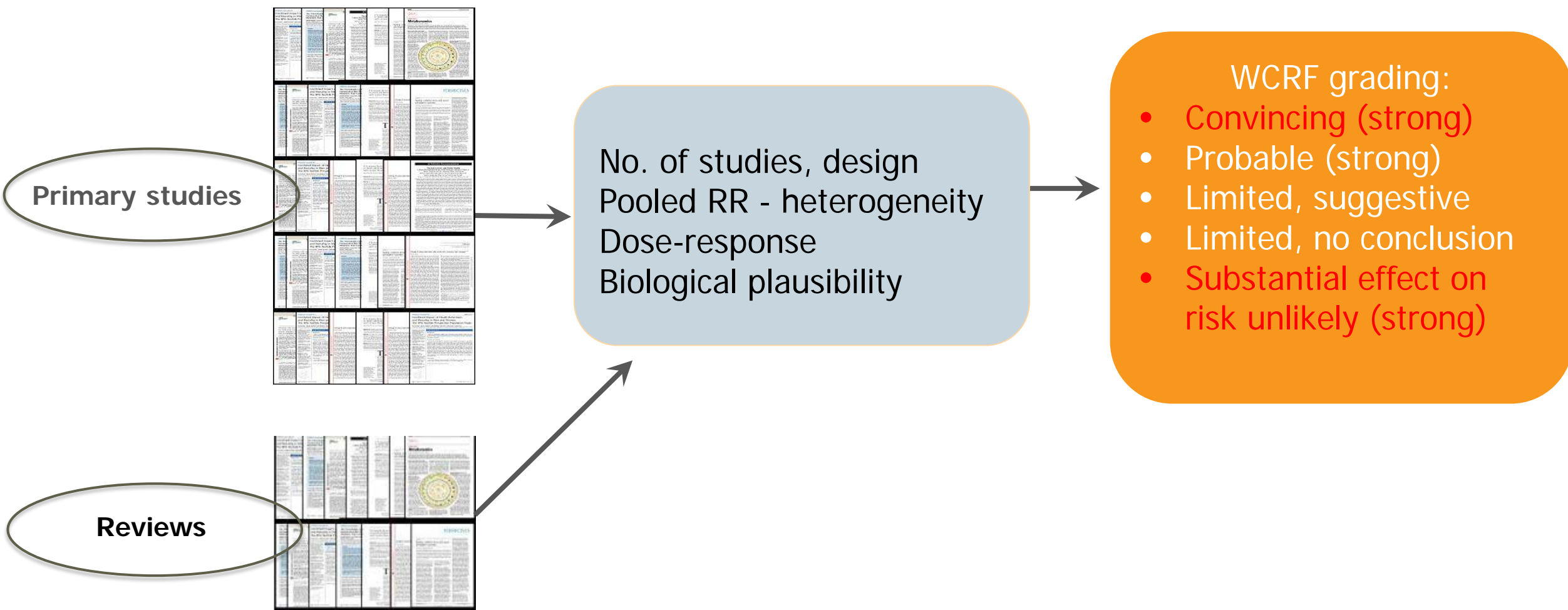
- **Systematic reviews**

- AMSTAR tool

- **Primary studies**

- Cross-sectional design used as exclusion criteria, no RoB
- Templates from Nordic Nutrition Recommendations (NNR) 2012 for
 - Case-control
 - Prospective cohort
 - Nested case-control
 - RCT
- Overall grade A, B or C. Studies graded C were excluded.

Grading of evidence – WCRF criteria (2018)



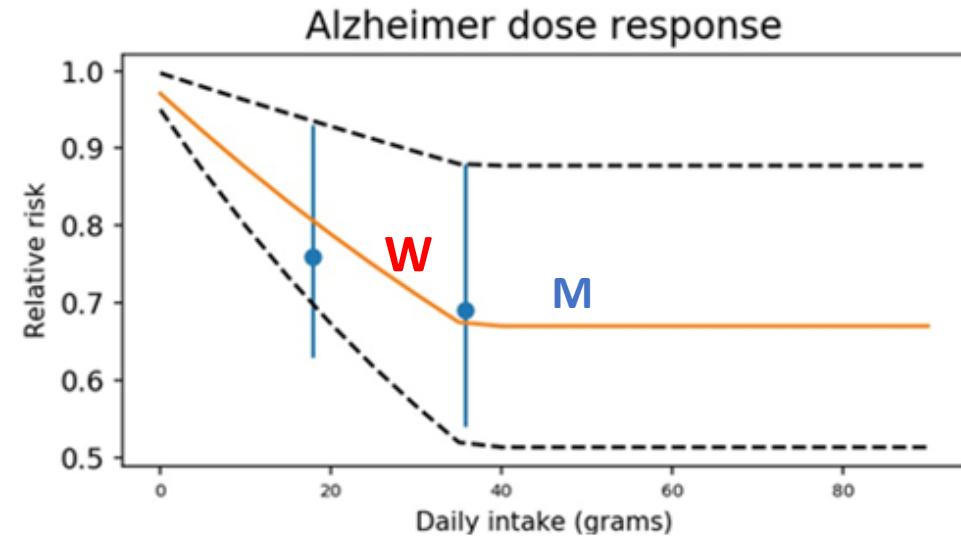
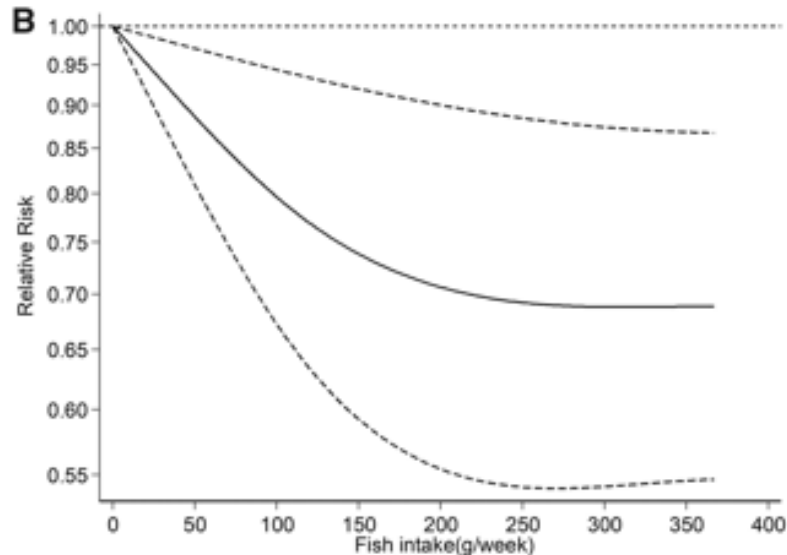
WCRF = World Cancer Research Fund

Modelling example – fish intake and Alzheimer’s

Meta-dose response analysis (7 studies) by Kosti 2022:

Weighted mixed-effects model with restricted cubic splines, 3 knots at fixed percentiles of fish intake)

Loglinear model fitted to the reported relative risks



Kosti et al. 2022: *Nutrition Reviews*, Volume 80, Issue 6, June 2022, p 1452

Current mean population fish intake:

Men= 50 g/d, Women = 34 g/d

Example: Potential impact fractions (PIF) or percent change in annual number of new cases estimated for change in fish intakes from the current intake to 150, 300 or 450 g/week

Health outcome	Men (350 g/wk)			Women (238 g/wk)		
	Scenario 1 150 g/wk	Scenario 2 300 g/wk	Scenario 3 450 g/wk	Scenario 1 150 g/wk	Scenario 2 300 g/wk	Scenario 3 450 g/wk
Alzheimer's	16% (5.2, 28)	0% (0, 0)	0% (0, 0)	13.95% (4.6, 24.2)	-1.76% (-2.9, -0.6)	-1.76% (-2.9, -0.6)
New cases (70-90+ yrs)	+416	0	0	+481	-61	-61

- The numbers in brackets indicate the estimated PIF using the lower and upper limits of the 95% confidence intervals around the relative risks.
- A negative sign indicates an expected percentwise decrease in number of cases

Some challenges in assessment

- Different body of epi evidence on fish, nutrients and contaminants
 - Differences in study designs, health outcomes and population groups
 - E.g. mostly observational studies for fish intake, and mostly RCTs for nutrients (dietary supplement intake)
 - How to weigh benefits and risk considering these differences
- Large body of evidence for fish/nutrients and health
 - How to synthesize evidence from multiple/independent reviews
 - RoB assessment becomes very time consuming

Which RoB tools should we use in future assessments?

- Nordic Nutrition Recommendations 2023 implemented other tools*
 - RCTs: RoB 2 from Cochrane
 - Nutrition Observational Studies: (RoB-NObs) from the USDA
 - Nutrition Evidence Systematic Review team
 - Non-randomized intervention studies: ROBINS-I
 - (ROBINS-E for effects of exposure not available at the time)
- Other options
 - OHAT (US National Toxicology Program)
 - raROB (BfR)

*Arnesen EK et al. The Nordic Nutrition Recommendations 2022 - handbook for qualified systematic reviews. Food Nutr Res. 2020 Jun 18;64. PMID: 32612492

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The logo for VKM, consisting of the letters 'VKM' in a bold, black, sans-serif font. A thin horizontal line is positioned below the letters.

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A close-up photograph of a hand reaching down to touch a stalk of wheat. The scene is bathed in warm, golden light, likely from the setting or rising sun, creating a soft glow and lens flare effects. The wheat stalks are in sharp focus in the foreground, while the background is blurred.

Thank you for your attention!

The VKM logo, consisting of the letters 'VKM' in a bold, black, sans-serif font, positioned in the bottom right corner of the slide.

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