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Vitenskapskomiteen for mattrygghet
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Assessment of zinc intake in relation to tolerable upper intake levels

Opinion of the Panel on Nutrition, Dietetic Products, Novel Food and Allergy of the Norwegian Scientific Committee for Food Safety

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Assessment of zinc intake in relation to tolerable upper intake levels

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Competence of VKM experts

Persons working for VKM, either as appointed members of the Committee or as external experts, do this by virtue of their scientific expertise, not as representatives for their employers or third party interests. The Civil Services Act instructions on legal competence apply for all work prepared by VKM.

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Summary

The Norwegian Food Safety Authority (NFSA, Mattilsynet) has requested the Norwegian Scientific Committee for Food Safety (VKM) to assess the intake of iron zinc in the Norwegian population in relation to tolerable upper intake levels (ULs). The existing maximum limit for zinc in food supplements is 25 mg/day.

VKM has also conducted scenario calculations to illustrate the consequences of amending the maximum limit to 1, 2, 5, 10, 15 or 20 mg/day.

Zinc is an essential trace element required for RNA, DNA and protein synthesis, cellular division, differentiation and growth (MacDonald, 2000). Zinc is required for catalytic function in several enzymes and participates in all major biochemical pathways in the body. The function of the immune system depends on the ability of its cells to proliferate and differentiate, which is impaired in individuals with suboptimal zinc status (Barton et al., 2000). Due to its role in cell division and differentiation, adequate zinc nutrition is particularly important in children, and the requirements per kg body weight are highest in early life. The endogenous intestinal losses can vary from 7 mmol/day (0.5 mg/day) to more than 45 mmol/day (3 mg/day), depending on zinc intake (King and Turnlund, 1989).

The requirements for zinc vary according to age and bioavailability. Several bioactive compounds in food such as tannins and phytic acids interact with zinc absorption and increase zinc requirements. The requirements vary twenty-fold according to life stage and diet.

Zinc supplements, even at or slightly above the recommended intakes, can cause nausea and vomiting. The main concern with chronic zinc excess is, however, copper deficiency which is associated with several chronical illnesses. However, copper deficiency is uncommon due to the ubiquitous presence of copper in the diet.

VKM proposes to use the ULs set by IOM (2001) as they provide values also for children and adolescents. The tolerable upper intake level set for adults is 40 mg zinc per day from food (and water) and supplements.

Based on the scenario estimations, a dietary zinc intake at the 95th percentile and additionally 20 mg zinc from food supplements will lead to an intake close to the tolerable upper intake level established by IOM for adults. For adolescents and child populations the maximum amounts are 15 and 5 mg for 13- and 9-year-olds, respectively. For 2 and 4-year-olds, P95 from intake of zinc from food alone exceeds the UL.

Key words: VKM, risk assessment, Norwegian Scientific Committee for Food Safety, zinc, food supplement, upper level, exposure.

Sammendrag på norsk

Vitenskapskomiteen for mattrygghet har vurdert inntak av sink i den norske befolkningen i relasjon til øvre tolerable inntaksnivåer (UL). Den eksisterende maksimumsgrensen for sink i kosttilskudd er 25 mg/dag. VKM har også gjort scenarioberegninger for å illustrere konsekvensene av å endre denne maksimumsgrensen for sink til 1, 2, 5, 10, 15 eller 20 mg/dag i kosttilskudd.

Sink er et essensielt sporstoff som er nødvendig for RNA, DNA og proteinsyntese, celledeling, differensiering og vekst (MacDonald, 2000). Sink er nødvendig for katalytisk aktivitet i flere enzymer og inngår i alle viktige biokjemiske mekanismer i kroppen. Immunsystemet er avhengig av celledeling og differensiering, og dette svekkes i personer med suboptimal sink-status (Barton et al., 2000). På grunn av sin rolle i celledeling og differensiering, er det spesielt viktig at barn har et tilstrekkelig sinkinntak, og sinkbehovet uttrykt pr kg kroppsvekt er høyest hos de yngste. Ekskresjon via tarm kan variere fra 7 mmol/døgn (0,5 mg/dag) til mer enn 45 mmol/dag (3 mg/dag), avhengig sinkinntaket (King and Turnlund, 1989).

Kroppens behov for sink varierer med alder og biotilgjengeligheten. Flere bioaktive forbindelser i mat som for eksempel tanniner og fytater hemmer sinkabsorpsjonen som igjen medfører behov for et høyere inntak. Behov for sink kan variere med en faktor på tjue, avhengig av livsfase og kosthold.

Kosttilskudd med sink kan forårsake kvalme og oppkast, selv i doser som ligger på anbefalt inntak. Hovedproblemet med kronisk forhøyet inntak av sink er imidlertid kobbermangel som er assosiert med flere kroniske sykdommer. Kobbermangel er imidlertid uvanlig ettersom det er rikelig med kobber i kosten.

VKM foreslår å bruke de tolerable øvre inntaksnivåer (tolerable upper intake levels; ULs) fastsatt av Institute of Medicine (IOM), USA i 2001. De har også inkludert øvre inntaksnivåer for barn og unge. Tolerabelt øvre inntaksnivå for voksne er 40 mg sink per dag fra mat (og vann) og kosttilskudd.

I henhold til scenarioberegningene, vil et kosttilskudd med 20 mg sink per dag i tillegg til inntak av sink fra kosten hos 95-persentilen føre til et sinkinntak nært opptil det tolerable øvre inntaksnivået som IOM har fastsatt for voksne. For ungdom og barn kan sinktilskudd maksimum inneholde henholdsvis 15 og 5 mg for 13- og 9-åringer. For 2 og 4-åringer er sinkinntaket i 95-persentilen fra kosten alene over de fastsatte tolerable øvre inntaksnivåene for disse aldersgruppene.

Abbreviations and/or glossary

Abbreviations

EFSA	– European Food Safety Authority
ESOD	– copper-containing enzyme in erythrocytes
EVM	– Expert group on vitamins and minerals of the Food Standard Agency, UK
LOAEL	– lowest observed adverse effect level
NFSA	– Norwegian Food Safety Authority [*Norw.*: Mattilsynet]
NHMRC	– National Health and Medical Research Council (Australia and New Zealand)
NNR	– Nordic Nutrition Recommendations
NOAEL	– no observed adverse effect level
IOM	– Institute of Medicine, USA
RCT	– randomised controlled trial
RI	– recommended intake
UF	– uncertainty factor
UL	– tolerable upper intake level
VKM	– Norwegian Scientific Committee For Food Safety [*Norw.*: Vitenskapskomiteen for Mattrygghet]

Glossary

P5, 25, 50, 75 or 95-exposure is the calculated exposure at the 5, 25, 50, 75 or 95-percentile.

Percentile is a statistical measure indicating the value below which a given percentage of the observations fall. E.g. the 95-percentile is the value below which 95 percent of the observations are found.

Average Requirement (AR) is the level of intake of a defined group of individuals estimated to satisfy the physiological requirement of metabolic demand, as defined by a the specific criterion for adequacy for the nutrient, in half of the heathy individuals in a life stage or sex group, on the assumption that the supply of other nutrients and energy is adequate.

Recommended Intake (RI) is defined as the amount of a nutrient that meets the known requirement and maintains good nutritional status among practically all healthy individuals in a particular life stage or gender group. $RI = AR + 2SD_{AR}$.

Tolerable Upper intake Level (UL) is the maximum level of total chronic daily intake of a nutrient (from all sources) judged to be unlikely to pose a risk of adverse health effects to humans.

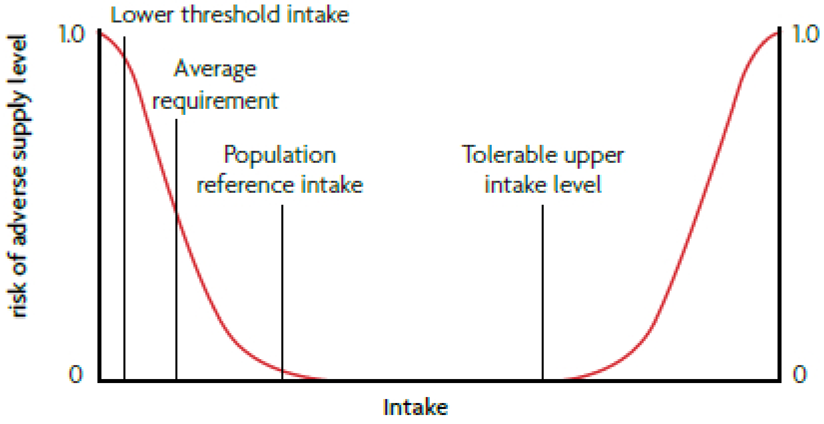

Figure 2: Relationship between individual intake and risk of adverse effects due to insufficient or excessive intake using EFSA terminology.

Background as provided by the Norwegian Food Safety Authority

Directive 2002/46/EC on food supplements was implemented in Norwegian law in 2004 in Regulation 20 May 2004 No. 755 on food supplements. Pursuant to Directive 2002/46/EC, common maximum and minimum levels of vitamins and minerals in food supplements shall be set in the EU.

National maximum limits for vitamins and minerals were established in the former vitamin and mineral supplements regulation from 1986 and were continued in the 2004 regulation.

The European Commission started establishing common limits in 2006, but the work was temporarily put on standstill in 2009. The time frame for the further work is not known.

Maximum limits for levels of vitamins and minerals in food supplements shall be set on the basis of the following criteria, pursuant to article 5 in Directive 2002/46/EC:

- Upper safe levels of vitamins and minerals established by scientific risk assessment based on generally accepted scientific data, taking into account, as appropriate, the varying degrees of sensitivity of different consumer groups
- Intake of vitamins and minerals from other dietary sources

When the maximum levels are set, due account should also be taken of reference intakes of vitamins and minerals for the population.

Pending establishment of common maximums limits in the EU, the Norwegian Food Safety Authority is evaluating the national maximum limits for vitamins and minerals in food supplements.

Assessment of zinc

The Norwegian Food Safety Authority will evaluate the national maximum limits for zinc in the food supplement regulation. The minimum and maximum limits for the content of vitamins and minerals in food supplements are listed in Annex 1 to the food supplement regulation:

Background Table: Minimum and maximum limits for zinc in the food supplement regulation (May 2016).

	Minimum amount per recommended daily dose	Maximum amount per recommended daily dose
Zinc (mg)	4	25

Permitted zinc substances which may be used in the manufacture of food supplements are listed in Annex 2 in the food supplement regulation.

Terms of reference as provided by the Norwegian Food Safety Authority

The Norwegian Food Safety Authority (NFSA, Mattilsynet) requests the Norwegian Scientific Committee for Food Safety (VKM) to assess the intake of zinc from the diet, including fortified products, in all age groups in the population above 1 year (mean, P5, P50 and P95).

VKM is also requested to conduct scenario estimations to illustrate the consequences of amending maximum limits for zinc to 1, 2, 5, 10, 15 or 20 mg/day in food supplements, and to evaluate these scenarios against already established tolerable upper intake levels.

Assessment of zinc

1 Introduction

Zinc is an essential trace element required for RNA, DNA and protein synthesis, cellular division, differentiation and growth (MacDonald, 2000). Zinc is required for catalytic function in many enzymes and participates in all major biochemical pathways in the body. It is also important for the structure and function of cellular membranes (Cousins et al., 2006). Cells with a rapid turnover, such as those of the epithelial linings of the gastrointestinal and respiratory tracts, are particularly sensitive to zinc deficiency (Hambidge, 2000). The function of the immune system depends on the ability of its cells to proliferate and differentiate, which is impaired in individuals with suboptimal zinc status (Barton et al., 2000). Natural killer cell activity, the chemotactic response of monocytes, and macrophage function, which are important in the initial phases of the immune response, are impaired in zinc deficiency (Shankar and Prasad, 1998). Studies in zinc deficient animals and children have reported substantial thymic atrophy, and consequently reduced T cell numbers in the blood and peripheral lymphoid tissues and impaired T cell dependent immunity (Shankar and Prasad, 1998). Animal studies show that B cell development and antibody responses are impaired in zinc deficiency (Shankar and Prasad, 1998). Due to its role in cell division and differentiation, adequate zinc nutrition is particularly important in children, and the requirements per kg body weight are accordingly highest in early childhood.

Oral zinc given to children with diarrhoea reduces the duration and the risk of persistence (Lukacik et al., 2008). A similar preventive effect is seen when oral zinc is given routinely. Long term zinc administration is also proven to reduce the incidence of pneumonia. These effects are well established and oral zinc is now recommended by the World Health Organization (WHO) for the treatment of childhood diarrhea.

The endogenous intestinal losses of zinc vary from 7 mmol/day (0.5 mg/day) to more than 45 mmol/day (3 mg/day), mostly depending on zinc intake (King and Turnlund, 1989). Zinc is absorbed throughout the small intestine and the absorption is dependent on the concentration in the intestinal lumen. Zinc is lost through the intestines, urine and skin. Competitive interactions between zinc and other ions with similar physicochemical properties can affect the uptake and intestinal absorption of zinc (Bhandari et al., 2002; Walsh et al., 1994). The risk for competitive interactions seems mainly to be related to high doses in the form of supplements or in aqueous solutions. However, at levels present in food, zinc absorption appears not to be affected, for example, by iron and copper (Sandstrom and Lonnerdal, 1989).

1.1 Requirements and recommended intakes

The requirements for zinc vary according to age and bioavailability. Several bioactive compounds in the diet such as tannins and phytic acids interact with zinc absorption and accordingly increase zinc requirements. The requirements vary twentyfold according to life stage and bioavailability of the diet. Due to its role in cell division and differentiation, adequate zinc nutrition is particularly important in children.

Zinc supplements, even at or slightly above the recommended intakes, can cause nausea and vomiting (Bahl et al., 2002; Bhandari et al., 2002; Strand et al., 2002). These immediate adverse reactions are usually most prominent at the first day of administration, and can be reduced by dividing the daily dose into two or more administrations.

In 2004, Nordic Nutrition Recommendations (NNR Project Group, 2012) estimated that the average dietary requirements (AR) for zinc was 6.4 mg and 5.7 mg for men and women, respectively. Using an inter-individual variation in requirement of 15%, the recommended intakes (RIs) were set to 9 mg/day for men and 7 mg/day for women. In NNR 2012, the RIs from 2004 were kept unchanged, since no new scientific data that justify a change has emerged (see Table 1.1-1). The physiological zinc requirements and endogenous losses for children and adolescents are higher than those of adults. The RIs for children and adolescents per body weight are therefore higher than for adults. These values were also presented in NNR 2004 and were not changed in the 2012 report because of no new data.

Table 1.1-1: Recommended intakes of zinc according to age and gender (NNR Project Group, 2012).

Age, both sexes	Zinc, mg/day	
	Men	Women
6-11 mo.	5	5
1-2 years	5	5
2-5 years	6	6
6-9 years	7	7
10-13 years	11	8
14-17	12	9
18-30	9	7
31-60	9	7
61-64	9	7
≥75 years	9	7
Pregnant		9
Lactating		11

The Norwegian recommendations for zinc are based on the NNR (2012).

2 Tolerable upper intake levels

Tolerable upper intake levels for zinc have been established by several authorities; IOM, USA (2001), Scientific Committee for Food, EU (2002), Expert Group on Vitamins and minerals (EVM), UK (2003), Australian National Health and Medical Research Council (NHMRC) (2005) and European Food Safety Authority (2005).

Institute of Medicine (IOM, 2001), USA

The UL for adults was primarily based on a lowest observed adverse effect level (LOAEL) of 60 mg/day derived from a study in 18 healthy women (aged 25 to 40 years) who were supplemented daily for 10 weeks (Yadrick et al., 1989). The main outcome of this randomised controlled trial (RCT) was erythrocyte superoxide dismutase activity, an enzyme that is dependent on adequate zinc and copper status. The LOAEL of 60 mg/day was calculated by adding a rounded estimate of dietary intake at 10 mg/day to the supplemental intake of 50 mg/day. Support for a LOAEL of 60 mg/day was provided by other studies showing altered copper balance after zinc supplementation (Fischer et al., 1984 cited in IOM, 2001).

An uncertainty factor (UF) of 1.5 was selected to account for interindividual variability in sensitivity and for extrapolation from a LOAEL to a no observed adverse effect level (NOAEL). Because reduced copper status is rare in humans, a higher UF was not justified. Using a UF of 1.5 resulted in a UL of 60/1.5= 40 mg/day.

IOM based the UL for infants from a NOAEL derived from a randomised controlled trial (RCT) in 68 young infants that were supplemented with zinc for 6 months. The observed NOAEL of 4.5 mg/day zinc did not alter plasma copper or cholesterol concentration, nor did it cause other adverse effects. Rounding down and using an UF of 1 resulted in a UL of 4 mg/day for infants. It was stated that the length of the study and the high number of infants justified a UF of 1.0, given that there was no evidence that intakes from formula of 5.8 mg/L of zinc result in infant toxicity. The UL for other childhood age groups as well as for pregnant and lactating women were extrapolated from the UL in young infants.

Scientific Committee for Food (SCF, 2003), EU

The ULs in the report from SCF (2003) are based on a NOAEL of 50 mg/day when estimating several of endpoints including the effect of zinc on the plasma concentration of copper. An uncertainty factor of 2 was used because the studies had relatively few participants and limited follow-up time. The ULs for children and adolescent were extrapolated according to body weight.

Expert Group on Vitamins and Minerals (EVM, 2003), UK

The EVM-report mainly based their upper levels on the same studies as IOM and NHMRC, but argues that there is no evidence for adverse effects from dietary zinc intake, and that the dietary zinc data in the relevant studies are uncertain. The EVM-report therefore concluded that it was appropriate to establish upper levels for supplemental, but not total, zinc intake. The UL from the EVM report is 25 mg/day or 0.42 mg/kg bw per day. The report gave no specific guidelines for children or adolescents.

In the EVM-report it is stated that "The key endpoint is the reduction of copper absorption by zinc. Where the contribution of dietary zinc was also assessed, the lowest level at which effects were apparent (reduced activity of the copper-dependent enzyme ESOD being the most sensitive) was approximately 58-62 mg/day (50 mg supplements plus approximately 8-12 mg/day from food). There is no evidence of adverse effects from dietary zinc intake. In addition, since the contribution of zinc from the diet in many of the studies is uncertain, and may have been altered under study conditions, it is appropriate to set a safe upper level for supplemental zinc but not total intake. Taking the LOAEL as 50 mg/day and by applying an uncertainty factor of 2 to account for LOAEL to NOAEL extrapolation, a Safe Upper Level of 50/2 = 25 mg/day for supplemental zinc is derived (equivalent to 0.42 mg/kg bw per day in a 60 kg adult). An uncertainty factor of 2 has been used since the effect concerned is a small and inconsistent change in a biochemical parameter. No uncertainty factor is needed for inter-individual variability because this safe upper level is supported by a large number of human studies."

Australian National Health and Medical Research Council (NHMRC, 2005)

Nutrient Reference Values (NRVs) from the Australian National Health and Medical Research Council (NHMRC) and the New Zealand Ministry of Health (MoH) was published in a report in 2005 where UL for zinc was included. They derived their ULs using the same studies and methods as in the IOM report, and arrived at almost identical values.

2.1.1 Summary and discussion tolerable upper intake level

The ULs from SCF, IOM and NHMRC apply for intakes from both food (and water) and food supplements, whereas the upper levels set by EVM apply for supplements alone. All the upper levels have identified measures for secondary copper deficiency as critical endpoints.

Table 2.1.1-1 gives an overview of the risk characterisation for upper levels for adults.

Table 2.1.1-1: Overview of risk characterisation for upper levels in adults set by various authorities.

	UL mg/day	Mainly based on	NOAEL mg/day	LOAEL mg/day	UF
IOM, 2000	40	2 human key studies		60	1.5
SCF, 2003	25	4 human studies	50		2
EVM, 2003	25 for supplemental zinc only	5 human key studies		50	2
NHMRC, 2005	40	2 human key studies		60	1.5

VKM acknowledges that several studies have reported adverse effects on measures relevant for secondary copper deficiency at supplemental intakes of 50 mg zinc per day. VKM therefore does not support the SCF-report that has considered 50 mg/day as a NOAEL.

The IOM and NHMRC-reports have identical approaches and results for all age groups. They have included zinc from food and water, and their ULs apply for total zinc intake from all sources. They argue that "Although there are no data indicating adverse interactions between zinc and other nutrients when zinc is found in food, adverse nutrient interactions are present after feeding zinc in the form of dietary supplements."

The IOM and NHMRC ULs for children are based on a study in infants and adjusted for body weights.

The EVM-report has mainly based its upper levels on the same studies as IOM and NHMRC, but argued that there is no evidence for adverse effects from dietary zinc intake, and that the dietary zinc data in the relevant studies are uncertain. The EVM-report therefore concluded that it was appropriate to establish upper levels for supplemental, but not total, zinc intake. In the EVM-report no data is given for children or adolescents.

Table 2.1.1-2 summarises available upper intake levels for zinc in various age groups.

Table 2.1.1-2: Summary of different upper levels for zinc.

	IOM, 2001	SCF, 2003	EVM, 2003*	NHMRC, 2006
Children, mg/day	7 (1-3 yr)	7 (1-3 yr)		7 (1-3 yr)
Children, mg/day	12 (4-8 yr)	10 (4-6 yr)		12 (4-8 yr)
Children, mg/day		13 (7-10 yr)		
Adolescents, mg/day	23 (9-13 yr)	18 (11-14 yr)		25 (9-13 yr)
Adolescents, mg/day	34 (14-18 yr)	22 (15-17 yr)		35 (14-18 yr)
Adults, mg/day	40 (19 yr+)	25 (18 yr +)	25 (18 yr+)	40 (19 yr+)

*Applies for supplements only.

VKM proposes to use the ULs set by IOM (2001)/NHMRC (2005) which provide values also for children and adolescents.

3 Intakes and scenarios zinc

In the terms of reference, VKM is requested to assess the intake of zinc from the diet, including fortified products, in all age groups in the population above 1 year. VKM is also requested to conduct scenario estimations to illustrate the consequences of amending maximum limits for zinc in food supplements zinc to 1, 2, 5, 10, 15 or 20 mg/day in food supplements.

3.1 Short description of the Norwegian dietary surveys

The estimated intakes of zinc presented in this opinion are based on data from the national food consumption surveys for young children (2-year-olds), children and adolescents (4, 9- and 13-year-olds) and adults (aged 18 to 70 years). The national food consumption surveys were conducted by the Department of Nutrition, University of Oslo in collaboration with the Directorate of Health, the Norwegian Food Safety Authority and the Norwegian Institute of Public Health. Different methodologies were used in the three different surveys and thus direct comparisons between the age groups may be misleading.

A description of the food consumption surveys and the different methodologies used is given below.

Adults: "Norkost 3" is based on two 24-hour recalls by telephone at least one month apart. Food amounts were presented in household measures or estimated from photographs (Totland et al., 2012). The study was conducted in 2010/2011, and 1787 adults (925 women and 862 men) aged 18-70 participated.

9- and 13-year-old children/adolescents: "Ungkost 3" is based on a 4-day food intake registration with a web based food diary. All food items in the diary were linked to photographs for portion estimation (Hansen et al., 2016). The study was conducted in 2015 and 636 9-year-old children and 687 13-year-old adolescents participated.

4-year-old children: "Ungkost 3" is based on a 4-day food intake registration with a web based food diary. All food items in the diary were linked to photographs for portion estimation (Hansen et al., 2017). The study was conducted in 2016, and 399 4-year-olds participated.2-year-old children: "Småbarnskost 2007" is based on a semi-quantitative food frequency questionnaire. In addition to predefined household units, food amounts were also estimated from photographs. The study was conducted in 2007, and a total of 1674 2-year-olds participated (Kristiansen et al., 2009).

3.2 Dietary intakes of zinc in the Norwegian population

Intakes of zinc in the various age groups and in groups of users of zinc supplements are presented in tables in Appendix 1. The tables in Appendix 1 also include calculations for P25 and P75.

Adults

The mean intake of zinc from the diet alone is 11.5 mg /day (median 10.9 mg/day) in adults (n=1787). The P5 intake is 5.8 mg/day and the P95 intake is 19.9 mg/day.

In Norkost 3, 285 participants (16%) reported use of zinc-containing supplements. Their mean total intake of zinc including that from food supplements is 20.6 mg/day (median 18.6 mg/day), P5 intake is 9.1 mg/day and P95 intake is 35.6 mg/day.

Mean intake of zinc from supplements alone in adults reporting use of zinc-containing supplements is 9.5 mg/day (median 7.5 mg/day), P5 intake is 1.1 mg/day and P95 intake is 22.5 mg/day.

13-year-olds (n=687)

The mean intake of zinc from the diet alone is 10.6 mg/day (median 10.1 mg/day) in 13-year-olds. The P5 intake is 5.4 mg/day and the P95 intake is 16.9 mg/day.

Twenty-three 13-year-olds (3%) reported use of zinc-containing supplements. Their mean total intake of zinc including that from food supplements is 14.7 mg/day (median 13.6 mg/day).

Mean intake of zinc from supplements alone in 13-year-olds reporting use of zinc-containing supplements is 3.9 mg/day (median 3.5 mg/day).

9-year-olds (n=636)

The mean intake of zinc from the diet alone is 9.6 mg/day (median 9.1 mg/day) in 9-year-olds. The P5 intake is 5.5 mg/day and the P95 intake is 15.5 mg/day.

Nineteen 9-year-olds (3%) reported use of zinc-containing supplements. Their mean total intake of zinc including that from food supplements is 13.6 mg/day (median 14.1 mg/day).

Mean intake of zinc from supplements alone in 9-year-olds reporting use of zinc-containing supplements is 4.1 mg/day (median 3.5 mg/day).

4-year-olds (n=399)

The mean intake of zinc from the diet alone is 7.5 mg/day (median 7.4 mg/day) in 4-year-olds. The P5 intake is 4.4 mg/day and the P95 intake is 11.2 mg/day.

Twenty-three 4-year-olds (6%) reported use of zinc-containing supplements. Their mean total intake of zinc including that from food supplements is 11.0 mg/day (median 10.5 mg/day).

Mean intake of zinc from supplements alone in 4-year-olds reporting use of zinc-containing supplements is 3.6 mg/day (median 2.5 mg/day).

2-year-olds (1674)

The mean intake of zinc from the diet alone is 6.5 mg /day (median 6.3 mg/day) in 2-year-olds. The P5 intake is 3.6 mg/day and the P95 intake is 10.2 mg/day.

None of the 2-year-olds reported use of zinc-containing supplements.

3.3 Scenario calculations for zinc

For scenario calculations VKM used the intakes of zinc from food alone in the P5 and P95 and added the suggested supplementation levels from NFSA (1, 2, 5, 10, 15 and 20 mg per day), see Tables 3.5-1 to 3.5-3.

Table 3.5-1 Calculated total zinc intakes for various age groups in scenarios with 1, 2, 5, 10, 15 and 20 mg as supplements added to the P5 intake from food alone (mg/day).

Age group	Intake in P5 from food	Including 1 mg from suppl	Including 2 mg from suppl	Including 5 mg from suppl	Including 10 mg from suppl	Including 15 mg from suppl	Including 20 mg from suppl
Adults	5.8	6.8	7.8	10.8	15.8	20.8	25.8
13 years	5.4	6.4	7.4	10.4	15.4	20.4	24.4
9 years	5.5	6.5	7.5	10.5	15.5	20.5	25.5
4 years	4.4	5.4	6.4	9.4	14.4	19.4	24.4
2 years	3.6	4.6	5.6	8.6	13.6	18.6	23.6

Table 3.5-2 Calculated total zinc intakes for various age groups in scenarios with 1, 2, 5, 10, 15 and 20 mg as supplements added to the P95 intake from food alone (mg/day).

Age group	Intake in P95 from	Including 1 mg from suppl	Including 2 mg from suppl	Including 5 mg from suppl	Including 10 mg from suppl	Including 15 mg from suppl	Including 20 mg from suppl
Adults	19.9	20.9	21.9	24.9	29.9	34.9	39.9
13 years	16.9	17.9	18.9	21.9	26.9	31.9	36.9
9 years	15.5	16.5	17.5	20.5	25.5	30.5	35.5
4 years	11.2	12.2	13.2	16.2	21.2	26.2	31.2
2 years	10.2	11.2	12.2	15.2	20.2	25.2	30.2

4 Assessment of the intakes of zinc

The ULs for zinc vary between the two main approaches that also included upper levels for children (SCF vs. IOM/NHMRC). In adults, these ULs are 25 or 40 mg/day, respectively, and the P95 intake of zinc from food alone is 20 mg/day. The UL set by SCF will therefore be exceeded with supplemental intakes at 10 mg/day while using the UL from IOM/NHMRC, the P95 intake will not exceed UL even at supplemental intakes of 20 mg/day.

VKM will use the ULs set by IOM (2001)/NHMRC (2005) at 40 mg zinc per day for adults. The ULs for children and adolescents are given in Table 2.1.1-2.

5 Uncertainties

It should be noted that the intakes have been calculated based on various dietary surveys for the different age categories and a comparison of calculations across age groups can be misleading. The calculated intakes in the higher and lower percentiles are always associated with a higher degree of uncertainty than mean or median intakes.

Thus, the percentile estimates of dietary intake are prone to random error due to the limited number of participants in the dietary surveys. The degree of uncertainty is largest in the estimated percentiles for 4-year-olds with a sample size of n=399, corresponding to about 20 observations below the 5-percentile and above the 95-percentile, respectively.

Another issue is that low participation limit the representativeness of the participants compared with the general background population in Norway. The participation among 13-, 9- and 4-year-olds in the dietary surveys were 53%, 55% and only 20%, respectively, while they were 37% in adults and 56% in 2-year-olds. In general, participants had considerably higher education level than the background population, and are expected to represent a health-conscious subgroup of the population. Some population subgroups are not covered, e.g. ethnic minorities. For the determinations of the ULs for zinc, EVM and IOM have not reached identical conclusions, indicating uncertainty regarding establishment of these ULs both for adults, children and adolescents.

The intake of zinc for 2-year-olds from the study Småbarnskost 2007, was originally calculated in the database (AE07) which do not contain zinc values for all foods. However, for the food codes used in the frequency questionnaire in Småbarnskost 2007 the coverage for zinc values were satisfactory, and the designated database AE07 was used.

The terms of reference has been to assess the intake in Norway in relation to already established tolerable upper intake levels which were established between 2001 and 2005. No literature search has been conducted for this VKM assessment and relevant recent evidence may accordingly not have been included.

6 Answers to the terms of reference

The Norwegian Food Safety Authority (NFSA, Mattilsynet) has requested the Norwegian Scientific Committee for Food Safety (VKM) to assess the intake of zinc from the diet, including fortified products, in all age groups in the population above 1 year in relation to tolerable upper intake levels (ULs).

VKM was also requested to conduct scenario estimations to illustrate the consequences of amending the existing maximum limit for zinc (to 1, 2, 5, 10, 15 or 20 mg/day, as examples) in food supplements. The existing maximum limit for zinc in food supplements is 25 mg/day.

In the assessment of zinc, VKM uses the tolerable upper intake levels established by IOM at 40 mg/day for adults.

Based on the scenario estimations, a dietary zinc intake at the 95th percentile and additionally 20 mg zinc from food supplements will lead to an intake close to the tolerable upper intake level established by IOM for adults. For adolescents and child populations the maximum amounts are 15 and 5 mg for 13- and 9-year-olds, respectively. For 2 and 4-year-olds, P95 from intake of zinc from food alone exceeds the UL.

Table 6-1: An overview of the conclusions for zinc according to doses in supplements.
Green: No exceedance of the UL.
Red: Exceedance of the UL.

Doses in supplements / Age group	1 mg/day	2 mg/day	5 mg/day	10 mg/day	15 mg/day	20 mg/day
Adults	Green	Green	Green	Green	Green	Green
13 years	Green	Green	Green	Green	Green	Red
9 years	Green	Green	Green	Red	Red	Red
4 years	Red	Red	Red	Red	Red	Red
2 years	Red	Red	Red	Red	Red	Red

7 Data gaps

More age groups should be included in the dietary surveys in addition specific ethnic groups and other sub-populations.

In the chapter 5 we refer to the uncertainties setting ULs both for zinc. This refers to few clinical studies evaluating high intakes and different clinical endpoints.

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Appendix I

Summary tables of zinc intake for all age groups

Intakes of zinc in the various age groups are presented in the tables below. The tables summarise intakes from the diet alone, zinc containing supplements alone (users only) and total intakes from both diet and supplements (Tables 1-6). Intakes are also given for both genders.

Table 1 Zinc intakes from diet alone in various age groups (mg/day).

	Adults (n=1787)	13 years (n=687)	9 years (n=636)	4 years (n=399)	2 years (n=1674)
Zinc from diet alone, mean	11.5	10.6	9.6	7.5	6.5
Zinc from diet alone, median	10.9	10.1	9.1	7.4	6.3
Zinc from diet alone, P5	5.8	5.4	5.5	4.4	3.6
Zinc from diet alone, P25	8.5	8.0	7.5	6.1	5.1
Zinc from diet alone, P75	13.6	12.7	11.2	8.8	7.7
Zinc from diet alone, P95	19.9	16.9	15.5	11.2	10.2

Table 2 Zinc supplement users intake of total zinc from diet and supplements, and from supplements alone (users only), in various age groups (mg/day).

	Adults (n=285)	13 years (n=23)	9 years (n=19)	4years (n=23)	2 years (n=0)
Total zinc from diet and supplements, mean	20.6	14.7	13.6	11.0	
Total zinc from diet and supplements, median	18.6	13.6	14.1	10.5	
Total zinc from diet and supplements, P5	9.1	-	-	-	
Total zinc from diet and supplements, P25	14.5	-	-	-	
Total zinc from diet and supplements, P75	24.6	-	-	-	
Total zinc from diet and supplements, P95	35.6	-	-	-	
Zinc from supplements alone, mean	9.5	3.9	4.1	3.6	
Zinc from supplements alone, median	7.5	3.5	3.5	2.5	
Zinc from supplements alone, P5	1.1	-	-	-	
Zinc from supplements alone, P25	5.0	-	-	-	
Zinc from supplements alone, P75	12.5	-	-	-	
Zinc from supplements alone, P95	22.5	-	-	-	

Table 3 Zinc intakes from diet alone in various age groups, women/girls (mg/day).

	Women (n=925)	Girls 13 years (n=355)	Girls 9 years (n=341)
Zinc from diet alone, mean	9.8	9.5	8.9
Zinc from diet alone, median	9.4	9.2	8.4
Zinc from diet alone, P5	5.3	5.1	5.2
Zinc from diet alone, P25	7.6	7.2	7.1
Zinc from diet alone, P75	11.7	11.4	10.4
Zinc from diet alone, P95	15.3	15.2	13.8

Table 4 Zinc supplement users intake of total zinc from diet and supplements, and from supplements alone, in various age groups, women/girls (mg/day).

	Women (n=173)	Girls 13 years (n=14)	Girls 9 years (n=13)
Total zinc from diet and supplements, mean	18.6	14.4	12.6
Total zinc from diet and supplements, median	17.2	13.6	12.8
Total zinc from diet and supplements, P5	8.9	-	-
Total zinc from diet and supplements, P25	14.0	-	-
Total zinc from diet and supplements, P75	22.8	-	-
Total zinc from diet and supplements, P95	33.8	-	-
Zinc from supplements alone, mean	8.9	9.8	3.7
Zinc from supplements alone, median	7.5	8.6	3.5
Zinc from supplements alone, P5	1.5	-	-
Zinc from supplements alone, P25	5.0	-	-
Zinc from supplements alone, P75	12.5	-	-
Zinc from supplements alone, P95	23.3	-	-

Table 5 Zinc intakes from diet alone in various age groups, men/boys (mg/day).

	Men (n=862)	Boys 13 years (n=332)	Boys 9 years (n=295)
Zinc from diet alone, mean	13.4	11.8	10.5
Zinc from diet alone, median	12.8	11.4	10.0
Zinc from diet alone, P5	6.7	6.1	5.8
Zinc from diet alone, P25	10.1	9.0	8.3
Zinc from diet alone, P75	16.1	14.1	12.0
Zinc from diet alone, P95	21.6	18.3	16.2

Table 6 Zinc supplement users intake of total zinc from diet and supplements, and from supplements alone, in various age groups, men/boys (mg/day).

	Men (n=112)	Boys 13 years (n=9)	Boys 9 years (n=6)
Total zinc from diet and supplements, mean	23.6	15.2	15.8
Total zinc from diet and supplements, median	21.6	14.8	14.8
Total zinc from diet and supplements, P5	9.3	-	-
Total zinc from diet and supplements, P25	17.5	-	-
Total zinc from diet and supplements, P75	25.6	-	-
Total zinc from diet and supplements, P95	39.9	-	-
Zinc from supplements alone, mean	10.4	12.4	4.9
Zinc from supplements alone, median	7.5	11.9	5.0
Zinc from supplements alone, P5	0.9	-	-
Zinc from supplements alone, P25	5.0	-	-
Zinc from supplements alone, P75	12.5	-	-
Zinc from supplements alone, P95	22.5	-	-