# Zink- en Koperbepaling in bloed: methode en klinische betekenis

Critically Appraised Topic

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24 september 2024

ZIEKENHUIS

# Inhoud

- Inleiding: Rol van Koper en Zink in het menselijk lichaam
- Klinische waarde van koperconcentratie in serum
- Klinische waarde van zinkconcentratie in serum
- Met welk methode wordt de concentratie van zink en koper bepaald?

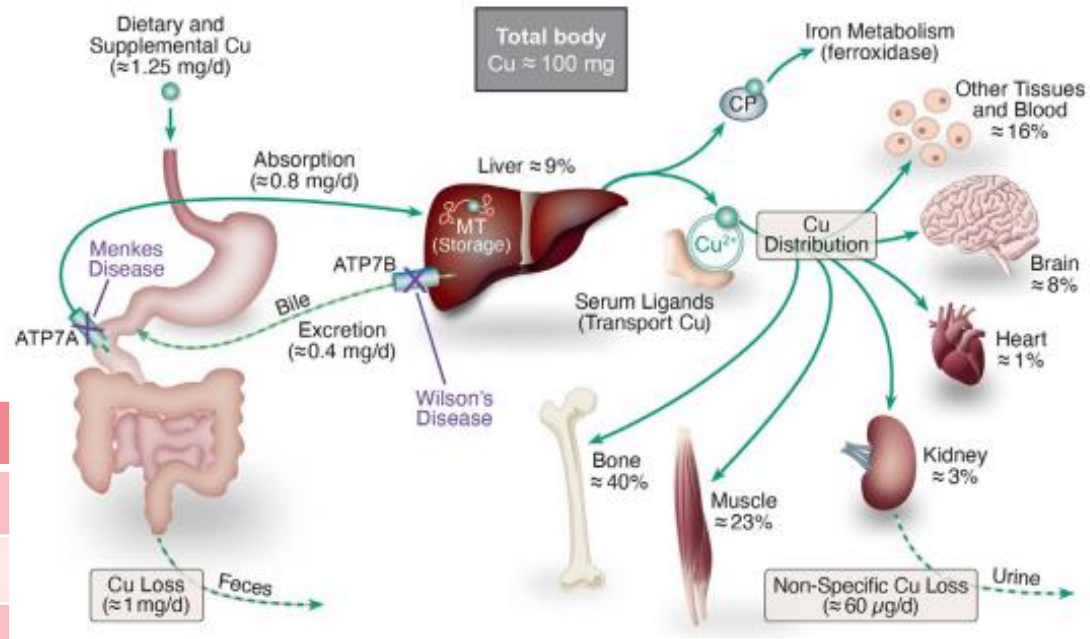
# Rol van koper en zink in het lichaam

# Koper in het menselijk lichaam

## Biologische functie

- Opname via darm en lever
  - Cupro-enzymes: ceruloplasmine
  - Cofactor enzymes
- Functie

| Koperafhankelijke enzymes | Functies |
|---|---|
| Ceruloplasmine | Koper- en ijzertransport |
| Lysyl oxidase | Collageen en elastine crosslinken |
| Cytochroom c oxidase | Mitochondriale energieproductie |
| Cu/Zn-Superoxidedismutase (SOD) | Antioxidant: detoxificatie vrije radicalen |
| Dopamine-beta-hydroxylase | Dopamine → Noradrenaline |
| Tyrosinase | Melanine synthese |



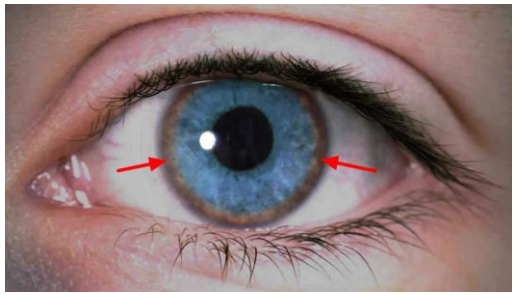


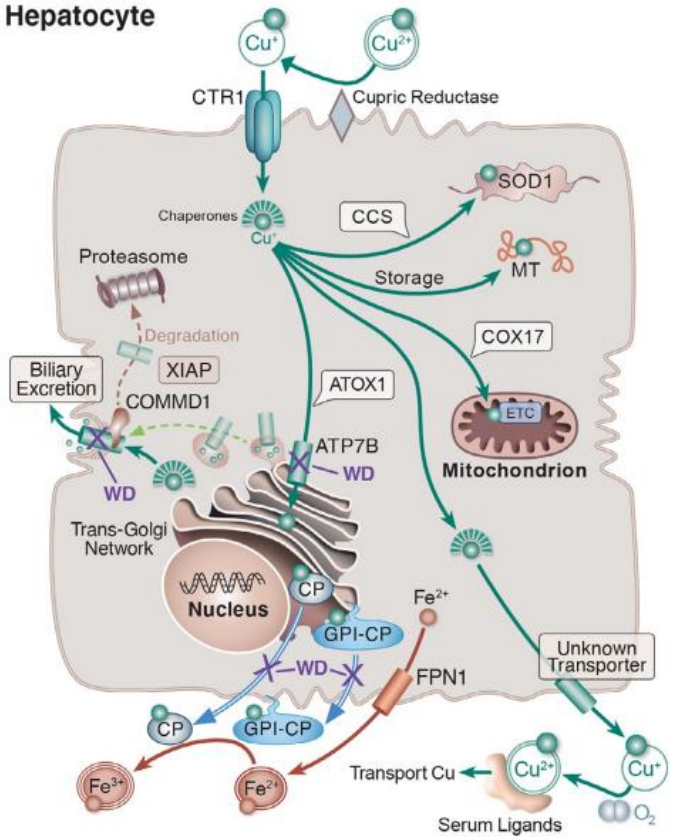

Collins JF. Copper nutrition and biochemistry and human (patho)physiology. 1st ed. Vol. 96, Advances in Food and Nutrition Research. Elsevier Inc.; 2021. 311–364 p.
Tabel obv: McArdle HJ. Principles of nutritional assessment. Copper. Vol. 3, Principles of nutritional assessment. 2023.

# Koper in het menselijk lichaam

## Erfelijke defecten koperhomeostase

- Ziekte van Menke
  - Defect absorptie
  - Ernstige symptomen
  - Levensverwachting <3 jaar
- Ziekte van Wilson
  - Defect excretie gal en inbouw cerul
  - Koperstapeling
  - Symptomen: hepatisch, neurologisch, Kayser-Fleischerringen








Collins JF. Copper nutrition and biochemistry and human (patho)physiology. 1st ed. Vol. 96, Advances in Food and Nutrition Research. Elsevier Inc.; 2021. 311–364 p.
Google afbeeldingen 'menkes kinky hair' op 18/09/2024 : ekşi sözlük - lütfen bekleyiniz (eksisozluk.com)
Google afbeelding 'kayser-Fleischer ring' op 18/09/2024 : Wilson's disease causes, symptoms, prognosis, diagnosis, test & treatment (healthjade.com)

# Koper in het menselijk lichaam

## Verworven aandoeningen

- **Koperdeficiëntie**
  - Anemie, Leukopenie
  - Neuropathie: myelo(neuro)pathie/optisch

- **Kopertoxiciteit**
  - Tot 1 g: gastro-intestinaal
  - Hoge dosissen: GI, hemolytische anemie, lever- en nierfalen, dood

| Oorzaken verworven koperdeficiëntie | |
|---|---|
| Verminderde intake | Armoede, anorexia<br>Enterale/parenterale voeding |
| Malabsorptie | Vegetarisch dieet (fytinezuren)<br>Inflammatoire darmziekten<br>Gastro-interestinale operaties<br>Zinktherapie |
| Verhoogde noden | Zwangerschap |
| Verhoogd verlies | Ernstige brandwonden<br>Dialyse |

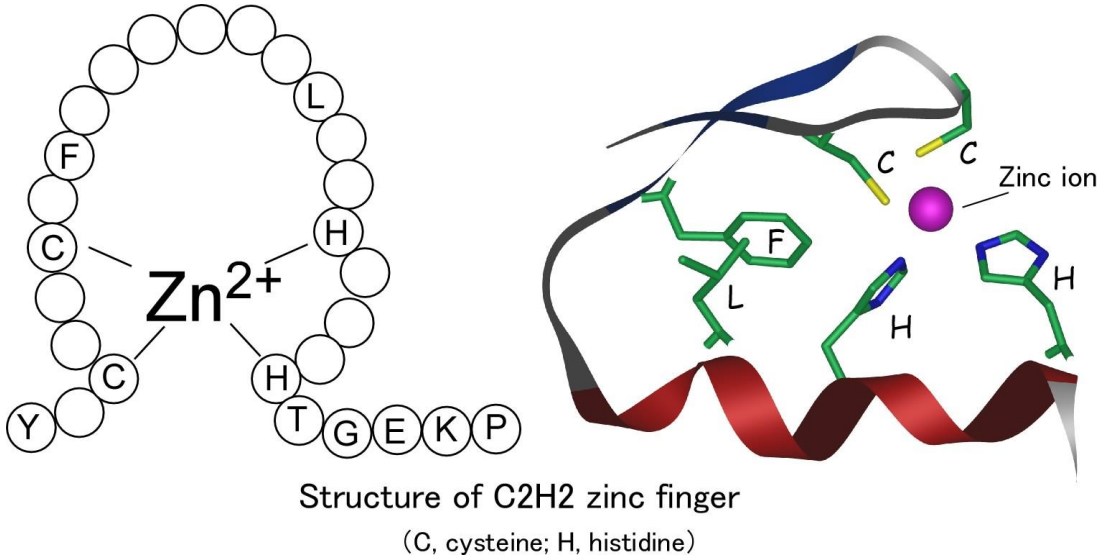
# Zink in het menselijk lichaam

## Biologische functies

- Intracellulair (99%)

- Katalyserende functie
- Structurele functie
- Regulatoire functie

→ Homeostase!




Structure of C2H2 zinc finger

(C, cysteine; H, histidine)



Google afbeeldingen 'zinc finger' op 18/09/2024 : www.med.nagasaki-u.ac.jp

# Zink in het menselijk lichaam

## Zinkdeficiëntie

- Acrodermatitis Enteropathica
  - Erfelijk <> verworven
  - Ernstige symptomen
- Verworven

| Oorzaken verworven zinkdeficiëntie | |
|---|---|
| Verminderde intake | Te weinig zink in dieet |
| Malabsorptie | Plantaardig dieet (fytinezuren)<br>IBS, coeliakie |
| Verhoogde noden | Zwangerschap<br>Borstvoeding<br>Groei |
| Verhoogd verlies | Acute diarree<br>Chronische nierinsufficiëntie<br>Diabetes mellitus<br>Sikkelcelanemie |

| Symptomen zinkdeficiëntie |
|---|
| Vertraagde wondheling |
| Verhoogde vatbaarheid infecties |
| Smaakstoornissen |
| Stomatitis |
| Vruchtbaarheid/zwangerschapsproblemen |
| Groeistoornissen |
| Diarree |
| Levercirrose |



Singh P, Nee J. BMJ Best Practice: Zinc deficiency.

# Zink in het menselijk lichaam

## Zinkexces

- **Acuut**
  - GI, hoofdpijn
- **Chronisch**
  - GI, verminderde immuunfunctie, daling HDL-cholesterol
  - Koperdeficiëntie

# Wat is de klinische waarde van de koperconcentratie in serum?

# Biomarker van de koperstatus

## Relatie koperintake

- Serum koper
  - Significante stijging serum koperconcentratie
  - Koper-status afhankelijk

→ Waarde als biomarker

Methods of assessment of copper status in humans: a systematic review[1–5]

*Linda J Harvey, Kate Ashton, Lee Hooper, Amélie Casgrain, and Susan J Fairweather-Tait*

*Harvey LJ, Ashton K, Hooper L, Casgrain A, Fairweather-Tait SJ. Methods of assessment of copper status in humans: A systematic review. Am J Clin Nutr. 2009;89(6).*

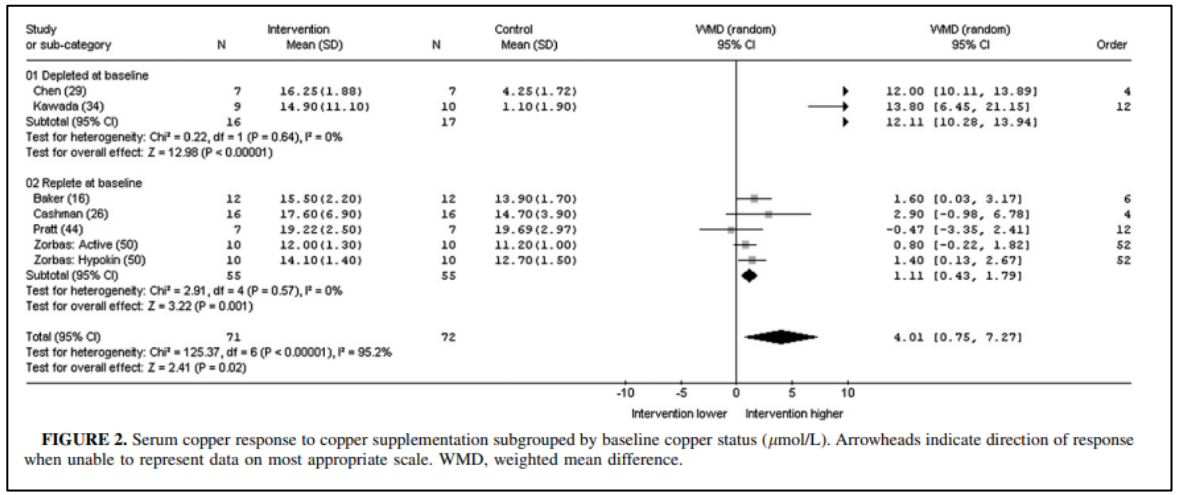



**FIGURE 2.** Serum copper response to copper supplementation subgrouped by baseline copper status (μmol/L). Arrowheads indicate direction of response when unable to represent data on most appropriate scale. WMD, weighted mean difference.



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# Biomarker van de koperstatus

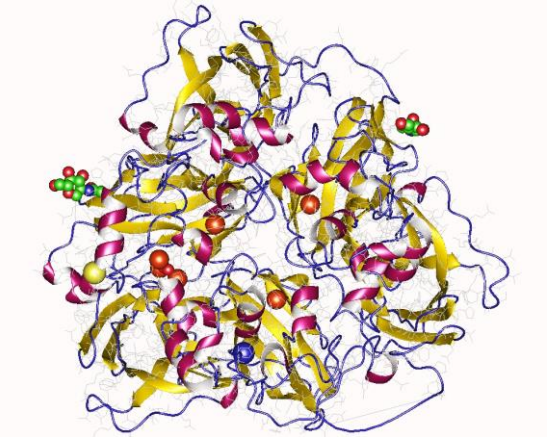
## Relatie ceruloplasmine

- 1 molecule ceruloplasmine

= 6-8 kopermoleculen

- 90% gebonden ceruloplasmine

→Stijgt en daalt samen



| Andere factoren die ceruloplasmine/koper beïnvloeden | |
|---|---|
| Infectie/inflammatie | Ceruloplasmine = acuut fase eiwit |
| Zwangerschap<br>Oestrogenen | Verhoogde ceruloplasminesynthese en -activiteit |
| Malnutritie, verminderde proteïnesynthese | Daling ceruloplasmine |

→Minder sensitieve parameter (zeker randverlaagd)



Google afbeeldingen 'ceruloplasmine structure' op 18/09/2024 : https://lookfordiagnosis.com/mesh_info.php?term=ceruloplasmin&lang=1

# Diagnose van koperdefiëntie

- Serum koper als screeningstest
- Ook ceruloplasmine en CRP

- Steeds andere deficiënties uitsluiten
  - Vb. Vitamine B12, ijzer…

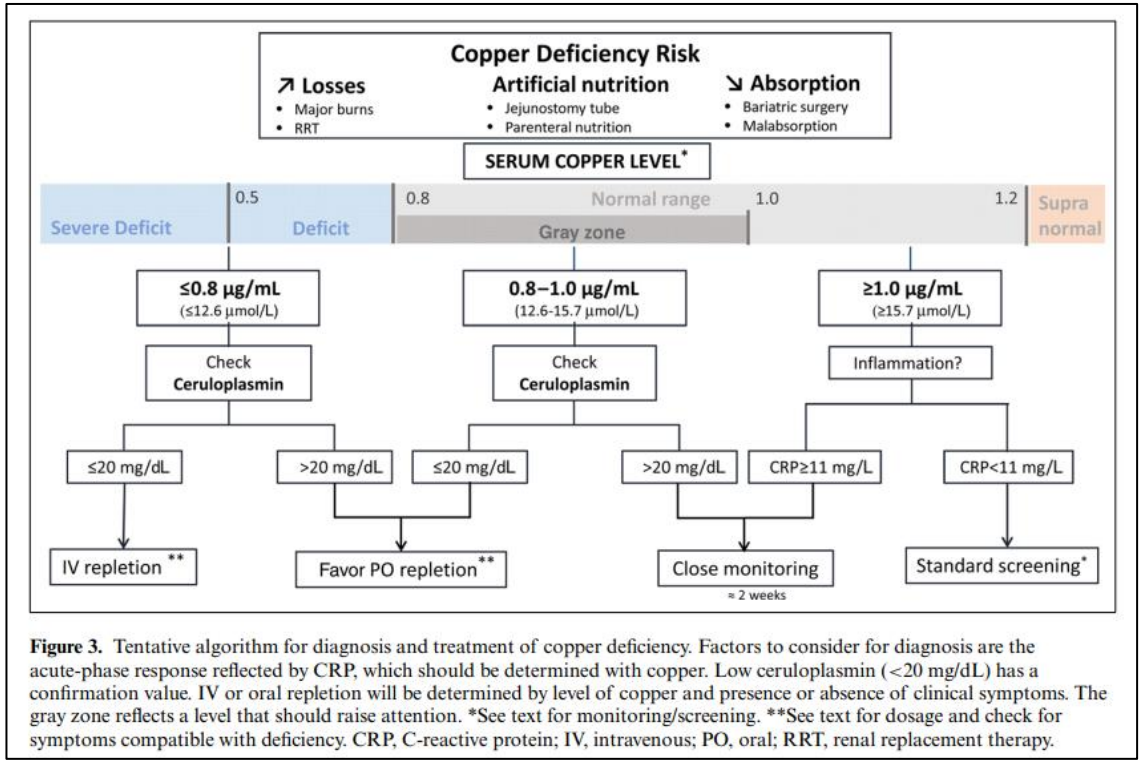



**Figure 3.** Tentative algorithm for diagnosis and treatment of copper deficiency. Factors to consider for diagnosis are the acute-phase response reflected by CRP, which should be determined with copper. Low ceruloplasmin (<20 mg/dL) has a confirmation value. IV or oral repletion will be determined by level of copper and presence or absence of clinical symptoms. The gray zone reflects a level that should raise attention. *See text for monitoring/screening. **See text for dosage and check for symptoms compatible with deficiency. CRP, C-reactive protein; IV, intravenous; PO, oral; RRT, renal replacement therapy.

Altarelli M, Ben-Hamouda N, Schneider A, Berger MM. Copper Deficiency: Causes, Manifestations, and Treatment. Nutr Clin Pract. 2019;34(4):504–13.

# Diagnose koperexces

- Niet ideaal→ teveel interferenties
- Verschillende cutoffs voor serum koper?
- Ook ifv intakes/symptomen
  - ADI: 5 mg/dag

**Re-evaluation of the existing health-based guidance values for copper and exposure assessment from all sources**

EFSA Scientific Committee,
Simon John More, Vasileios Bampidis, Diane Benford, Claude Bragard,
Thorhallur Ingi Halldorsson, Antonio F Hernández-Jerez, Susanne Hougaard Bennekou,
Kostas Koutsoumanis, Claude Lambré, Kyriaki Machera, Ewen Mullins, Søren Saxmose Nielsen,
Josef R Schlatter, Dieter Schrenk, Dominique Turck, Maged Younes, Polly Boon,
Gordon AA Ferns, Oliver Lindtner, Erik Smolders, Martin Wilks, Maria Bastaki,
Agnès de Sesmaisons-Lecarré, Lucien Ferreira, Luna Greco, George E N Kass,
Francesca Riolo and Jean-Charles Leblanc

More SJ, Bampidis V, Benford D, Bragard C, Halldorsson TI, Hernández-Jerez AF, et al. Re-evaluation of the existing health-based guidance values for copper and exposure assessment from all sources. EFSA J. 2023;21(1).

# Ziekte van Wilson

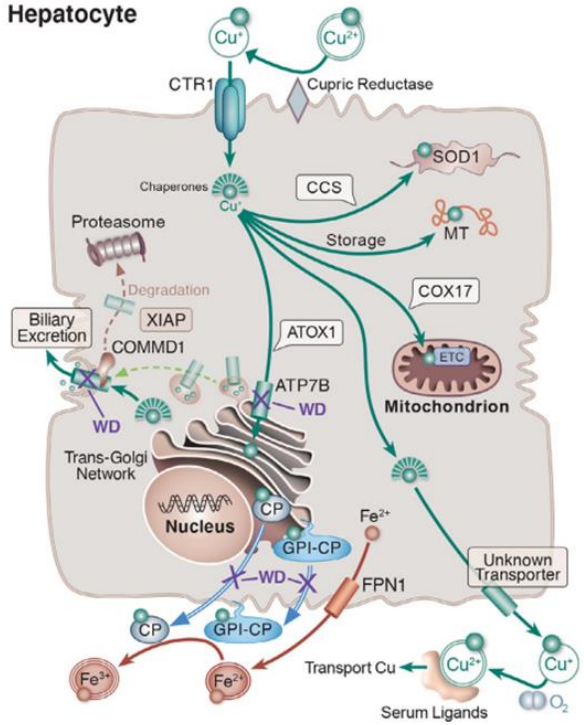
- Verlaagd!!
- Geen inbouw in ceruloplasmine

→(inactief) apoceruloplasmine wordt snel afgebroken → daling

| Andere factoren die ceruloplasmine/koper beïnvloeden | |
|---|---|
| Infectie/inflammatie | Ceruloplasmine = acuut fase eiwit |
| Zwangerschap<br>Oestrogenen | Verhoogde ceruloplasminesynthese en -activiteit |
| Malnutritie, verminderde proteïnesynthese | Daling ceruloplasmine |
| Acuut leverfalen, chronische cholestase | Verhoogde koperconcentratie |

→ Lage negatieve predictieve waarde

→ Hoge positieve predictieve waarde



# Ziekte van Wilson

## Algoritmes

**Table 4:** Leipzig scoring system for the diagnosis of Wilson's disease.[a]

| Symptoms, signs and tests (score) | |
|---|---|
| **Serum ceruloplasmin** | **Kayser-Fleischer rings:** |
| >0.2 g/L: 0 points<br>0.1–0.2 g/L: 1 point<br><0.1 g/L: 2 points | Present: 2 points<br>Absent: 0 points |
| **Urinary copper[b]** | **Neurological symptoms:** |
| Normal: 0 points<br>1–2× upper limit of reference: 1 point<br>>2× upper limit of reference: 2 points | Severe: 2 points<br>Mild: 1 point<br>Absent: 0 points |
| **Intrahepatic copper[c]** | **Mutation analysis[d]:** |
| >4 µmol/g (>250 µg/g): 2 points<br>0.8–4 µmol/g (50–250 µg/g): 1 point<br><0.8 µmol/g (<50 µg/g): −1 point | On both chromosomes: 4 points<br>On one chromosome: 1 point<br>No mutations: 0 points |
| **Coombs-negative hemolytic anemia** | **Overall score:** |
| Present: 1 point<br>Absent: 0 points | ≥4 points. Diagnosis established<br>3 points. Likely diagnosis<br>≤2 points. Very unlikely diagnosis |

[a]Modified from (19). [b]In absence of acute hepatitis. [c]In absence of cholestasis. [d]Detection of pathogenic or probably pathogenic variants.

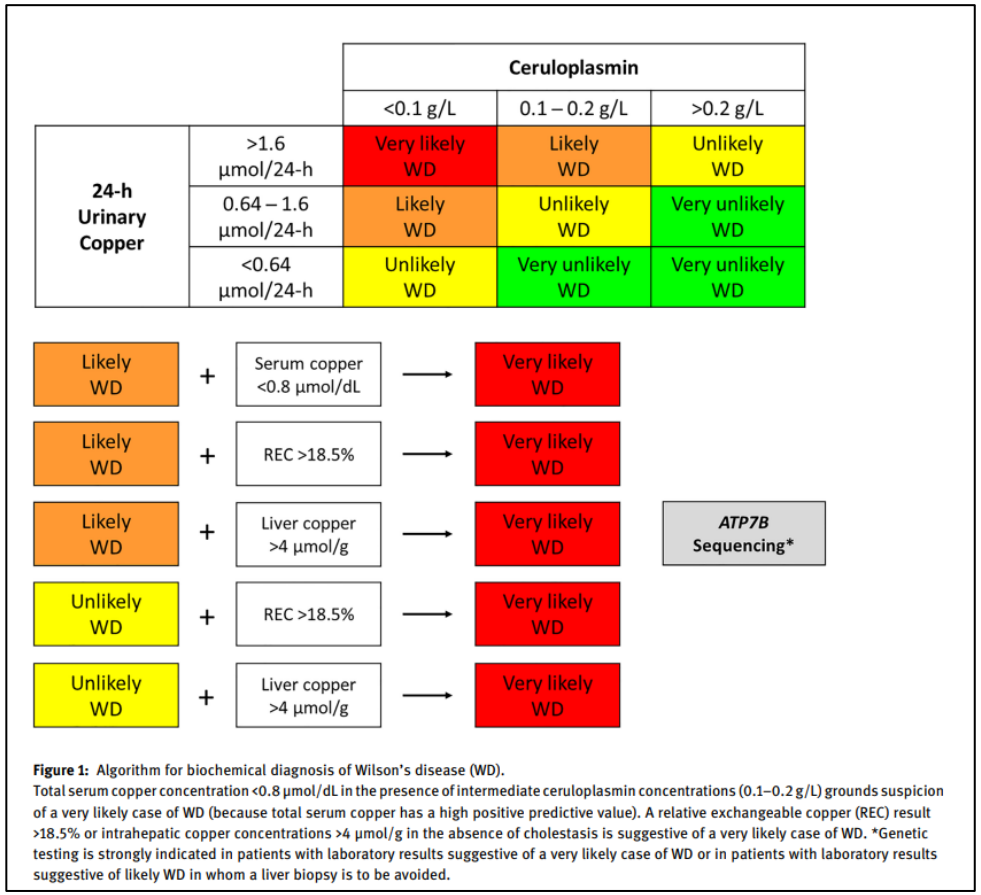



**Figure 1:** Algorithm for biochemical diagnosis of Wilson's disease (WD).
Total serum copper concentration <0.8 µmol/dL in the presence of intermediate ceruloplasmin concentrations (0.1–0.2 g/L) grounds suspicion of a very likely case of WD (because total serum copper has a high positive predictive value). A relative exchangeable copper (REC) result >18.5% or intrahepatic copper concentrations >4 µmol/g in the absence of cholestasis is suggestive of a very likely case of WD. *Genetic testing is strongly indicated in patients with laboratory results suggestive of a very likely case of WD or in patients with laboratory results suggestive of likely WD in whom a liver biopsy is to be avoided.



Martínez-Morillo E, Bauça JM. Biochemical diagnosis of Wilson's disease: An update. Adv Lab Med. 2022;3(2):103–13.
(19) Ferenci P, Caca K, Loudianos G, Mieli-Vergani G, Tanner S, Sternlieb I, et al. Diagnosis and phenotypic classification of Wilson disease. Liver Int 2003;23:139–42.

# Ziekte van Menke

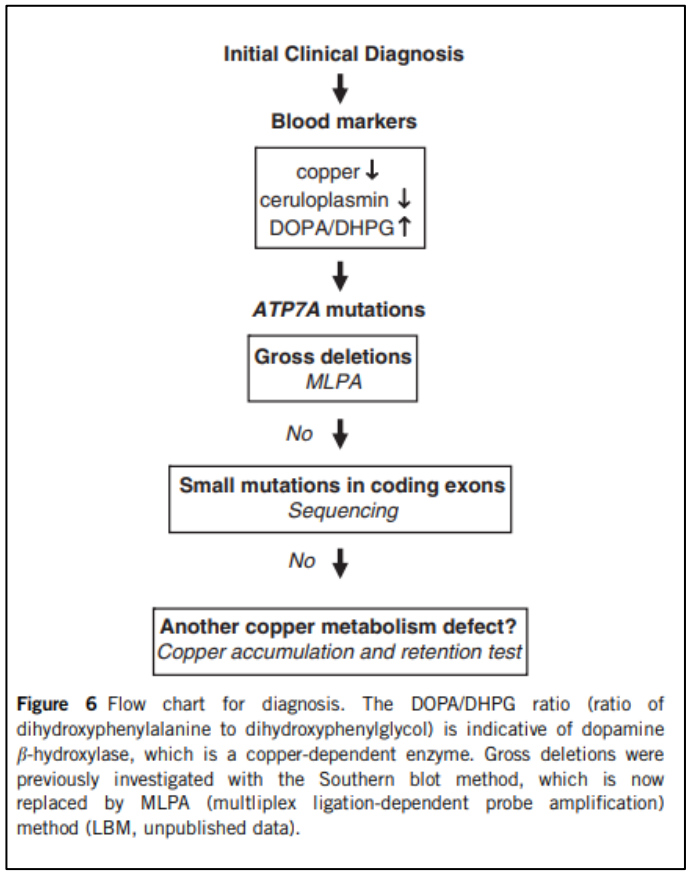



**Figure 6** Flow chart for diagnosis. The DOPA/DHPG ratio (ratio of dihydroxyphenylalanine to dihydroxyphenylglycol) is indicative of dopamine β-hydroxylase, which is a copper-dependent enzyme. Gross deletions were previously investigated with the Southern blot method, which is now replaced by MLPA (multiplex ligation-dependent probe amplification) method (LBM, unpublished data).

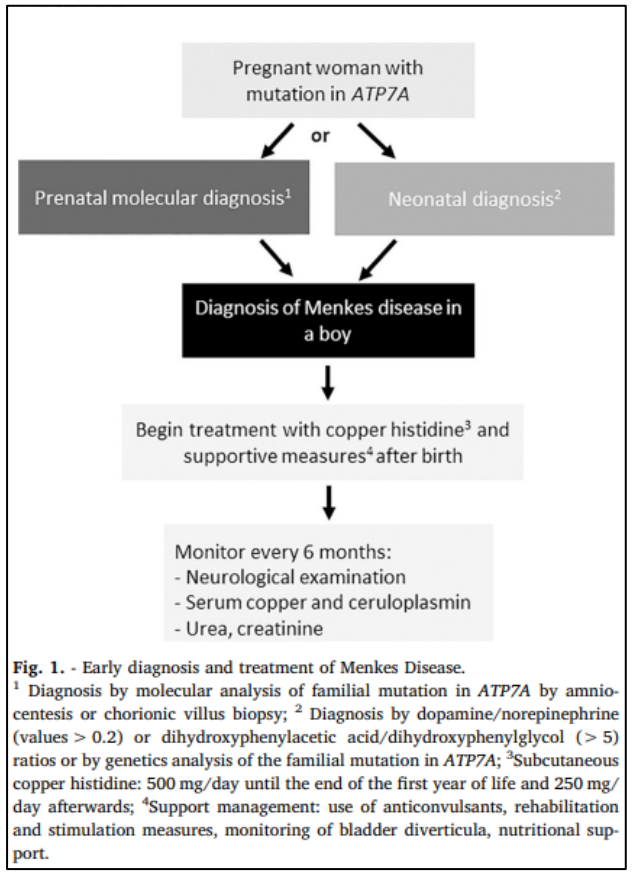



**Fig. 1.** - Early diagnosis and treatment of Menkes Disease.
[1] Diagnosis by molecular analysis of familial mutation in *ATP7A* by amniocentesis or chorionic villus biopsy; [2] Diagnosis by dopamine/norepinephrine (values > 0.2) or dihydroxyphenylacetic acid/dihydroxyphenylglycol (> 5) ratios or by genetics analysis of the familial mutation in *ATP7A*; [3]Subcutaneous copper histidine: 500 mg/day until the end of the first year of life and 250 mg/day afterwards; [4]Support management: use of anticonvulsants, rehabilitation and stimulation measures, monitoring of bladder diverticula, nutritional support.



Diagnose: Tümer Z, Møller LB. Menkes disease. Eur J Hum Genet. 2010;18(5):511–8.
Opvolging: Vairo FP e., Chwal BC, Perini S, Ferreira MAP, de Freitas Lopes AC, Saute JAM. A systematic review and evidence-based guideline for diagnosis and treatment of Menkes disease. Mol Genet Metab. 2019;126(1):6–13.

Jessa Ziekenhuis

# Wat is de klinische waarde van de zinkconcentratie in serum?

# Biomarker van de zinkstatus

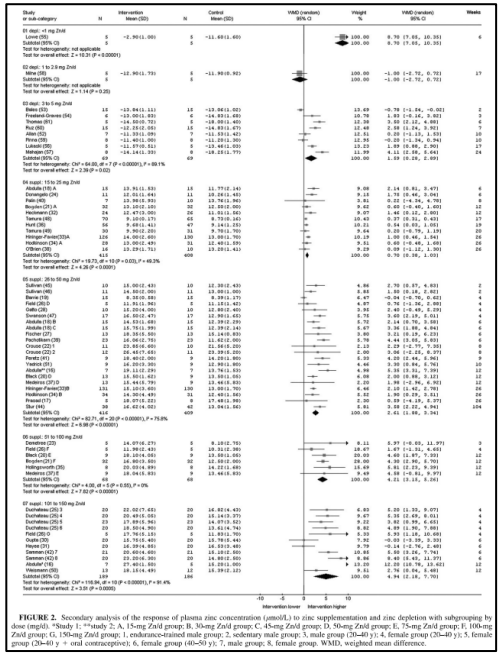
1. Relatie zinkintake

- Serum/plasma zink
  - 35 suppletiestudies
  - 10 depletiestudies
- Significante respons op intake
  - Grotere respons bij lagere baseline

Methods of assessment of zinc status in humans: a systematic review[1–5]

*Nicola M Lowe, Katalin Fekete, and Tamás Decsi*

*Lowe NM, Fekete K, Decsi T. Methods of assessment of zinc status in humans. Vol. 89 (suppl), The American journal of clinical nutrition. 2009. p. 1S-12S.*



# Biomarker van de zinkstatus

## 2. Relatie symptomen

- Cutoff: 50 µg/dL

The Journal of Nutrition
Nutrition and Disease

**Development of a Plasma Zinc Concentration Cutoff to Identify Individuals with Severe Zinc Deficiency Based on Results from Adults Undergoing Experimental Severe Dietary Zinc Restriction and Individuals with Acrodermatitis Enteropathica[1,2]**

K. Ryan Wessells,[3] Janet C. King,[4] and Kenneth H. Brown[3]*

[3]Department of Nutrition, University of California, Davis, Davis, CA; and [4]Children's Hospital Oakland Research Institute, Oakland, CA

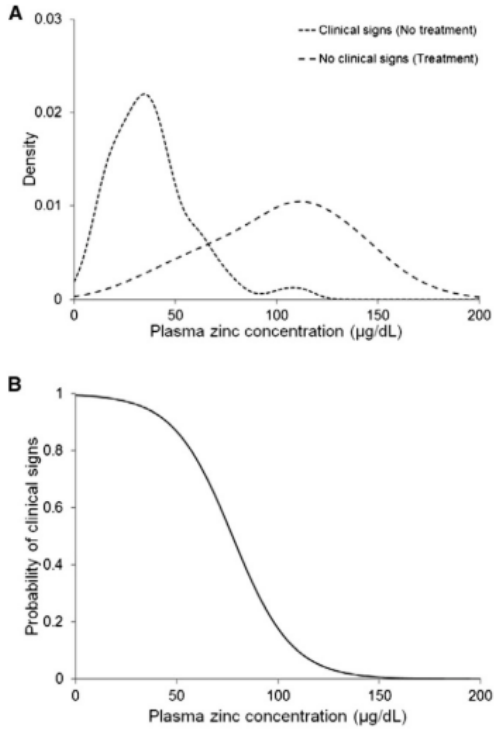



**FIGURE 3** Kernel density estimate plot of the distribution of plasma zinc concentrations among individuals with acrodermatitis enteropathica with ($n$ = 136) or without ($n$ = 56) clinical signs (*A*). Logistic regression of the relation between plasma zinc concentrations and the probability of clinical signs among the same set of individuals ($n$ = 192; 2 observations in 56 individuals) (*B*).

## 3. Functionele outcome suppletie

- Effect lengte/gewicht kinderen

Effect of supplemental zinc on the growth and serum zinc concentrations of prepubertal children: a meta-analysis of randomized controlled trials[1–3]

*Kenneth H Brown, Janet M Peerson, Juan Rivera, and Lindsay H Allen*

- Significante positieve respons van lengte en gewicht



Wessells KR, King JC, Brown KH. Development of a plasma zinc concentration cutoff to identify individuals with severe zinc deficiency based on results from adults undergoing experimental severe dietary zinc restriction and individuals with acrodermatitis enteropathica. J Nutr. 2014;144(8):1204–10.
Brown KH, Peerson JM, Rivera J, Allen LH. Effect of supplemental zinc on the growth and serum zinc concentrations of prepubertal children: A meta-analysis of randomized controlled trials1-3. Am J Clin Nutr. 2002;75(6):1062–71.

# Biomarker van de zinkstatus

## Tekortkomingen als biomarker

| Factoren die zinkconcentratie in serum/plasma beïnvloeden | |
|---|---|
| Dagelijkse variatie | Voedingsstatus, dag/nachtritme |
| Infectie/inflammatie | Daling albumine<br>Redistributie zink naar lever |
| Zwangerschap<br>Oestrogenen | Hemodilutie, daling zinkconcentratie |
| Malnutritie, verminderde proteïnesynthese | Daling albumine en zink |
| Hemolyse | Vrijkomen intracellulair zink |
| Contaminatie omgeving | Zinkcontaminatie door water, stof, afnamebuizen… |

→ Correctie obv CRP en alfa-1-acidglycoproteïne

→ pre-analyse!

→ Minder sensitieve parameter (voor milde deficiëntie)
Andere biomarkers?



IZiNCG. Adjusting plasma or serum zinc concentrations for inflammation. 2020;(10):1–6.

# Evaluatie zinkstatus populatie

- Zink concentratie in serum/plasma
  - >20% onder cutoff

  = gevaar volksgezondheid
- Verlaagde zinkintake
- Stunting

IZiNCG
WWW.IZING.ORG

The Journal of Nutrition
**Supplement: Biomarkers of Nutrition for Development (BOND) Expert Panel Reviews, Part 3**

**Biomarkers of Nutrition for Development (BOND)—Zinc Review[1–5]**

Janet C King,[6,7] Kenneth H Brown,[7,8] Rosalind S Gibson,[9] Nancy F Krebs,[10] Nicola M Lowe,[11] Jonathan H Siekmann,[6] and Daniel J Raiten[12]*

[6]Children's Hospital Oakland Research Institute, Oakland, CA; [7]University of California, Davis, Davis, CA; [8]Bill & Melinda Gates Foundation, Seattle, WA; [9]University of Otago, Dunedin, New Zealand; [10]University of Colorado School of Medicine, Aurora, CO; [11]University of Central Lancashire, Preston, United Kingdom; and [12]NIH, Bethesda, MD



IZiNCG. Promoting and assisting efforts to reduce global zinc deficiency.
King JC, Brown KH, Gibson RS, Krebs NF, Lowe NM, Siekmann JH, et al. Biomarkers of nutrition for development (BOND)-Zinc Review. J Nutr. 2016;146(4):858S-885S.

# Evaluatie zinkstatus individu

BMJ Best Practice

- Klinische evaluatie
  - Risicofactoren
  - Symptomen
- Zinkconcentratie in serum
  - 60 µg/dL / 70 µg/dL
- Andere deficiënties

BMJ Best Practice

Zinc deficiency

| Test | Result |
|---|---|
| **serum or plasma zinc levels**<br>• Serum and plasma zinc levels are the most commonly used tests and the only tests available in routine clinical practice. They are helpful in severe zinc deficiency but are less accurate in marginal deficiency partly due to issues with protein binding.[72] | **<60 micrograms/dL or <70 micrograms/dL in nonpregnant adults** |
| **serum iron level**<br>• Other nutrient deficiencies often coexist with zinc deficiency, including iron deficiency. | **low** |
| **serum 25-OH vitamin D level**<br>• Other nutrient deficiencies often coexist with zinc deficiency, including vitamin D deficiency.<br>• Although most labs report the normal range for 25-hydroxyvitamin D as 20 to 100 nanograms/mL, evidence supports the goal of >32 nanograms/mL based on calcium absorption and parathyroid hormone levels.[80] [81] | **<32 nanograms/mL** |
| **serum folate**<br>• Folate deficiency may coexist with zinc deficiency and testing or empiric supplementation should be considered, especially in women of childbearing age. | **<3 nanograms/mL (<7 nmol/L)** |
| **serum vitamin B12**<br>• Vitamin B12 deficiency may coexist with zinc deficiency. It may occur in individuals with disease affecting the ileum or in those with diets chronically very low in meat.<br>• Serum vitamin B12 <200 picograms/mL is highly suggestive of vitamin B12 deficiency and generally confirms the diagnosis. | **<200 picograms/mL** |

Singh P, Nee J. BMJ Best Practice: Zinc deficiency.

# Evaluatie zinkstatus individu

## Japan's Practical Guidelines

**Table 1.** The diagnostic guideline for zinc deficiency.

| **Zinc deficiency can be reliably diagnosed by the four criteria below:** |
|---|
| I. One or more symptoms and signs of zinc deficiency (dermatitis, aphthous stomatitis, hair loss, loss of appetite, taste disorder, hypogonadism in males, anemia, increased susceptibility to infection, growth disturbances in terms of weight and height in children, and low levels of serum alkaline phosphatase (ALP). However, serum ALP levels are not always low in patients with liver disease, osteoporosis, chronic kidney disease, or diabetes mellitus. |
| II. Ruling out of other diseases associated with the above symptoms or low serum ALP levels. For example, conditions such as contact dermatitis, atopic dermatitis, dermatitis due to deficiencies in vitamin A, biotin, or essential fatty acids, alopecia areata, hair-pulling, short stature due to growth hormone deficiency, familial short stature, Turner syndrome, and congenital hypophosphatasia should be ruled out. |
| III. Low serum zinc levels<br>III-1: <60 μg/dL: zinc deficiency<br>III-2: 60–80 μg/dL: marginal zinc deficiency<br>(Blood sampling is recommended in the morning under fasting conditions) |
| IV. Zinc treatment can be performed on patients who meet criteria I, II, and III. Symptoms in these patients can be improved with zinc treatment. |

International Journal of *Molecular Sciences*

MDPI

*Review*

**Japan's Practical Guidelines for Zinc Deficiency with a Particular Focus on Taste Disorders, Inflammatory Bowel Disease, and Liver Cirrhosis**

Hiroko Kodama [1,*], Makoto Tanaka [2], Yuji Naito [3], Kazuhiro Katayama [4] and Mitsuhiko Moriyama [5]

Ook suppletie bij normale zinklevels!

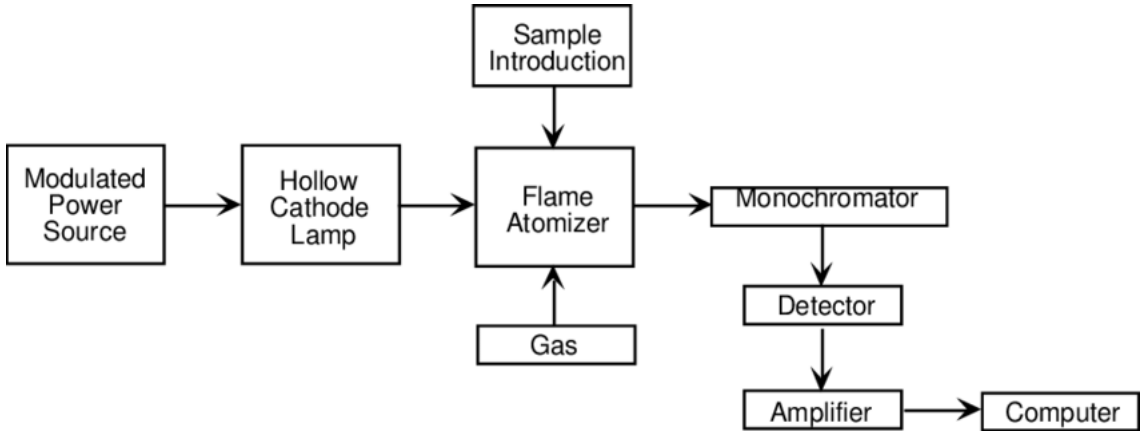


Kodama H, Tanaka M, Naito Y, Katayama K, Moriyama M. Japan's practical guidelines for zinc deficiency with a particular focus on taste disorders, inflammatory bowel disease, and liver cirrhosis. Int J Mol Sci. 2020;21(8):1–16.

# Met welke methode wordt de concentratie van zink en koper bepaald?

# Beschikbare methoden

## Atomaire absorptiespectrofotometrie (AAS)




- Interferenties
  - Vaste deelties: deuterium-achtergrondcorrectie
  - Achtergrondabsorptie: zeeman-achtergrondcorrectie
- Sensitiviteit: grafietoven

# Beschikbare methode

## Inductively coupled plasma – optical emission spectrometry (ICP-EOS/ICP-MS)

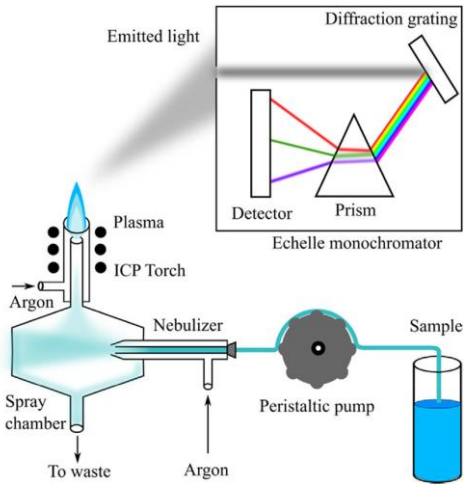



**Table 1:** Similarities and differences between instrument types used for zinc analysis

| | AAS | ICP-OES | ICP-MS |
|---|---|---|---|
| **Sample preparation** | Samples prepared in solution are fed into the instrument, energized, and the zinc content is measured based on emission or energy output | | |
| **What energizes the sample** | Flame or furnace | Plasma (hotter and more uniform than flame or furnace) generated by induction (using a magnetic field) | |
| **What is measured** | Optical emission (brightness) at the wavelength (color) for zinc | | Electrical emission of one or more zinc isotopes as they transition between ionized states in plasma |
| **Calibration method** | Zinc standard solution, at several known concentrations (calibrators), covering the range of likely zinc concentrations for the sample (i.e. standard curve calibration) | | |
| **Sensitivity** | Lowest | Intermediate | Highest |
| **Complexity and cost of operation** | Lowest | Intermediate | Highest |



Google afbeeldingen 'ICP' op 20/09/2024: https://www.researchgate.net/figure/A-simplified-scheme-showing-the-basic-operational-principles-of-ICP-OES_fig1_320140448

IZiNCG. Comparison of laboratory instrument types for analysis of plasma or serum zinc concentration. 2020.

# Beschikbare methode

Colorimetrisch

- Koper: 3,5-di-Br-PAESA
- Zink: 5-Br-PAPS

- Literatuur:
  - Beckett et al, 2009: methodevergelijking AAS
    → Koper: Significante systematische/fixed bias
    → Zink: Onzekerheid, bias
  - Handley SA et al, 2023: controles en methodevergelijking AAS en ICP-MS
    →Koper: Goede overeenkomst
    →Zink: Slechte overeenkomst interpretatie, veel variatie

**Evaluation of the Randox colorimetric serum copper and zinc assays against atomic absorption spectroscopy**

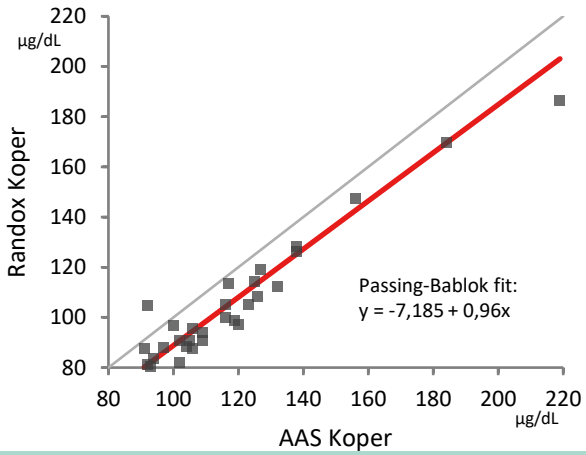
**Validation of the Randox colorimetric assays for serum copper and zinc**

# Evaluatie Randox kits

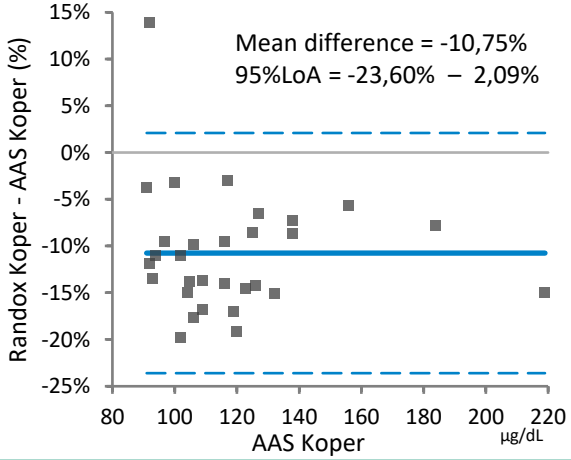
| Koper (µg/dL) | Repeteerbaarheid (within run) | | | | Reproduceerbaarheid (within lab) | | | | | | Juistheid | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Level 1 | | Level 2 | | Level 1 | | | Level 2 | | | Level 1 | | | | | | Level 2 | | | | | |
| | CV% | limiet | CV% | limiet | CV% | limiet | EFLM | CV% | limiet | EFLM | mean | target | lower limit | upper limit | bias (abs) % | EFLM | mean | target | lower limit | upper limit | bias (abs) % | EFLM |
| Randox | 2,29 | 2,87 | 1,61 | 2,80 | 2,11 | 5,52 | DES | 1,91 | 5,40 | DES | 97,6 | 104 | 85,6 | 122,4 | 6,13 | X | 145,7 | 117 | 96,3 | 137,7 | 24,56 | X |
| Seronorm | 2,4 | 2,84 | 1,43 | 2,32 | 2,3 | 5,48 | DES | 1,41 | 4,59 | OPT | 95,16 | 109,6 | 90,43 | 128,77 | 13,18 | X | 182,95 | 199,8 | 164,82 | 234,78 | 8,43 | X |

| Zink (µg/dL) | Repeteerbaarheid (within run) | | | | Reproduceerbaarheid (within lab) | | | | | | Juistheid | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Level 1 | | Level 2 | | Level 1 | | | Level 2 | | | Level 1 | | | | | | Level 2 | | | | | |
| | CV% | limiet | CV% | limiet | CV% | limiet | EFLM | CV% | limiet | EFLM | mean | target | lower limit | upper limit | bias (abs) % | EFLM | mean | target | lower limit | upper limit | bias (abs) % | EFLM |
| Randox | 0,44 | 1,79 | 0,92 | 1,66 | 2,79 | 5,60 | DES | 2,81 | 5,38 | DES | 180,1 | 222 | 183,5 | 260,5 | 18,86 | X | 217,5 | 242 | 199,1 | 284,9 | 10,12 | X |
| Seronorm | 0,49 | 2,34 | 1,7 | 1,99 | 4,02 | 6,42 | DES | 4,26 | 5,87 | DES | 121,23 | 145 | 119,04 | 170,96 | 16,39 | X | 167,6 | 196 | 161,21 | 230,79 | 14,49 | X |

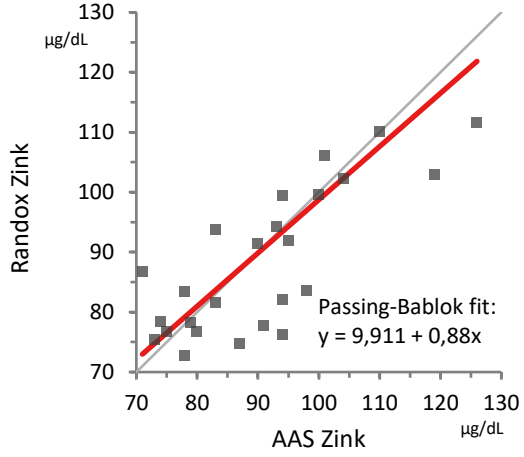
Passing-bablok



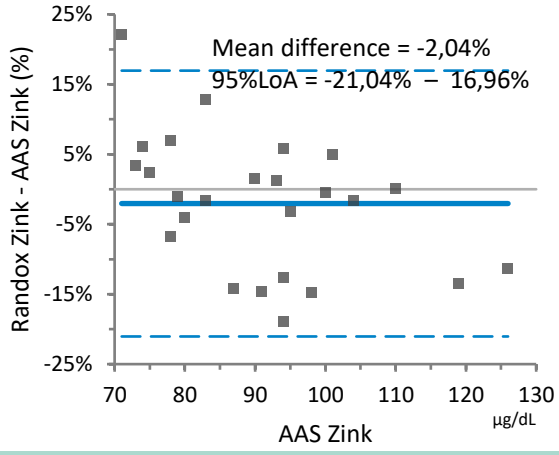

Bland-altman




Passing-bablok




Bland-altman



# Dank u wel!

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