

Vitamin E, Vitamin C, Zinc, & Chromium in diabetes

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American Diabetes Association

Standards of Care in Diabetes

01

Supplements have not been proven to be an effective option for lowering blood sugar or supporting diabetes management

02

For some patients may be necessary (deficiency, pregnant or breastfeeding, elderly, vegetarians, following very low-calorie or low-carbohydrate diets)



- ❖ The association between (E/C/Cr/Zn) and the risk of diabetes
- ❖ The role of (E/C/Cr/Zn) in glycemic control
- ❖ The prevalence of (E/C/Cr/Zn) deficiencies in diabetic patients
- ❖ The intake, absorption, metabolism, and excretion of (E/C/Cr/Zn) in diabetic patients
- ❖ Supplementation of (E/C/Cr/Zn)

Vitamin C

Intake

at the RDA level (70 mg/day)

↓ 24% risk of DM

Serum

65 $\mu\text{mol/l}$ VS 17 $\mu\text{mol/L}$

↓ 42% risk of DM

Supplement

(Lack of evidence)



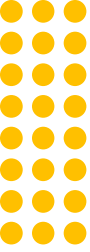
Lampousi A, et al.2024

Sun H, et al.2022

Li Z, et al.2025

Zheng Ju, et al. 2020

Neuenschwander M, et al. 2019

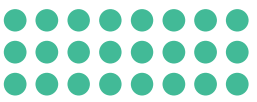


The role of Vit C in glycemic control

- ❖ Vitamin C can compete with glucose for binding to hemoglobin, HbA1C
- ❖ Translocation of Glut4
- ❖ Antioxidant

Liu j, et al.2023
Alberts A, et al. 2025
Undurty N, et al. 2019
Argano Ch, et al. 2025





Vitamin C status based on plasma concentration



Saturated
 $\geq 70 \mu\text{mol/L}$
 ≥ 170 Toxicity



Adequate
 $\geq 50\text{-}69 \mu\text{mol/L}$
(0.8-1.2 mg/dl)



**suboptimal status/
hypovitaminosis**
 $< 50\text{-}23 / < 23 \mu\text{mol/L}$
deficient
 $< 11 \mu\text{mol/L}$

Vitamin C deficiency in diabetic patients



***Diabetics have (30% & 5 $\mu\text{mol/L}$) lower serum vitamin C VS healthy people**

***Diabetics who are overweight, obese, or older have lower vitamin C levels**

***Prevalence of deficiency; 12–38%,**

***hypovitaminosis C $\geq$ 50-68%**

Car AC, et al.2023

Car AC, et al. 2024

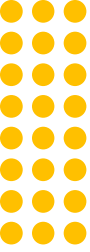
Car AC, et al.2022

Liu J et al.2023

Ebenuwa I, et al. 2022

Praveen D, et al.2020





Renal leak of vitamin C

01

Renal leak of vitamin C

dysregulation of the vitamin C transporter in the kidneys (SLC23A1) or damage to the renal tubules

02

Prevalence of vitamin C renal leak in diabetics: 33%

Estimated vitamin C intake required to achieve adequate plasma concentrations ($\geq 50 \mu\text{mol/L}$)



- *Healthy individuals: ~65–90 mg vitamin C/day**
- *Individuals with diabetes: ~125–166 mg vitamin C/day (approximately 1.5 times higher than in healthy individuals)**

Vitamin C supplementation

↓ FBS, HbA1c

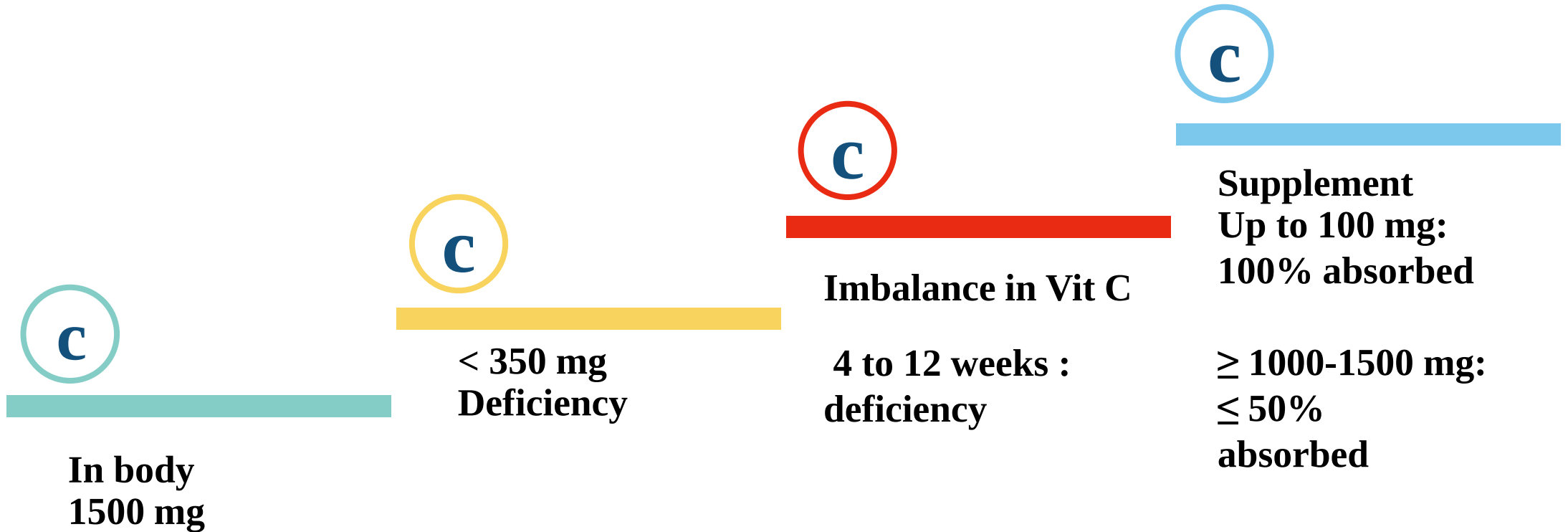
Long-term interventions are more beneficial

DFU



Rabizadeh S, et al. 2023
Mohammadi A, et al. 2023
Nosratabadi S, et al. 2023
Mason S, et al. 2022
Mason S, et al. 2021
Namkhah Z, et al. 2021
Das UN, et al. 2019
Liu J, et al. 2023
Lbban E, et al 2023
Tareke AB, et al. 2021

More information



RDA (C)

Age	Male	Female	Pregnancy	Lactation
0–6 months	40 mg*	40 mg*		
7–12 months	50 mg*	50 mg*		
1–3 years	15 mg	15 mg		
4–8 years	25 mg	25 mg		
9–13 years	45 mg	45 mg		
14–18 years	75 mg	65 mg	80 mg	115 mg
19+ years	90 mg	75 mg	85 mg	120 mg
Smokers	Individuals who smoke require 35 mg/day more vitamin C than nonsmokers.			

UL (C)

Age	Male	Female	Pregnancy	Lactation
0–12 months	Not possible to establish*		Not possible to establish*	
1–3 years	400 mg		400 mg	
4–8 years	650 mg		650 mg	
9–13 years	1,200 mg		1,200 mg	
14–18 years	1,800 mg		1,800 mg	1,800 mg
19+ years	2,000 mg		2,000 mg	2,000 mg



یک عدد (سایز متوسط)
گریپ فروت، پرتقال
یا کیوی



70
میلی گرم

نصف لیوان
توت فرنگی یا
آناناس



45
میلی گرم

نصف لیوان بروکلی پخته
یا یک لیوان کلم قرمز
خورد شده



55
میلی گرم

نصف لیوان
گل کلم پخته



30
میلی گرم

یک لیوان
کلم پیچ



85
میلی گرم

یک لیوان
جعفری



85
میلی گرم

یک عدد فلفل دلمه ای
سبز متوسط



95
میلی گرم

یک عدد فلفل دلمه ای
قرمز متوسط



150
میلی گرم

یک عدد سیب زمینی
متوسط پخته و یا یک عدد
گوجه فرنگی متوسط خام



17
میلی گرم

یک لیوان برگ شلغم
خورد شده



35
میلی گرم

Practical instructions



Reger D, et al. 2008
Maxfield L, et al. 2023
Thosar SS, et al. 2015
Park SW, et al. 2019
Gurreei A, et al. 2019
Shi C, et al. 2020

- **Nutritional: Fruit and vegetable intake status**
- **History** (Alcohol use disorder, Smoking, Bariatric surgery, Restrictive or low carbohydrate diets, Food allergies, mental illness, Hemodialysis, obesity)

- **Serum Vit C**

Supplementation:

- * 500 mg/d for 1 to 3 months
- * 2 g/d for the initial 3 days, 500 mg/d for 1 week, and 100 mg/d for 1 to 3 months

Diet: 125-165 mg/d (5 servings of fruits and vegetables provides about 200 mg of vitamin C)

Vitamin E



Intake

(High certainty)

At the RDA level (12 mg/day)

↓ 28% risk of DM

Serum

(Very low certainty)

High VS Low : ↓risk of DM

Supplement

(Moderate certainty)

No effect

Lampousi A, et al.2024

Valdes-Romas R, et al.2015

Liu S, et al.2006

The role of Vit E in glycemic control



- Antioxidant activity and reduction of oxidative stress
- Preservation of pancreatic β -cell function
- Inhibition of advanced glycation end-product (AGE) formation
- Activation of PPAR γ signaling and increased adiponectin secretion
- Reduction of inflammation and improvement of insulin sensitivity

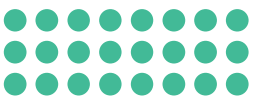
Balbi ME, et al. 2018

Bhatti JS, et al. 2022

Lee S, et al. 2024

Zaulkffali AS, et al. 2019

Lin B, et al. 2023



Vitamin E status based on plasma concentration



Toxicity: rare
(Supplement)



Adequate
5 to 15 $\mu\text{g/ml}$



deficiency
< 5 $\mu\text{g/ml}$
(<11.6–12 $\mu\text{mol/L}$)

In patients with extremely high or extremely low cholesterol levels, the levels of circulating alpha-tocopherol are not an accurate measure of vitamin E



Vitamin E deficiency in diabetic patients



- Diabetics have lower serum vitamin E
- women or older have lower vitamin E levels
- Prevalence of Vit E deficiency in healthy: 0.1% VS in diabetics: 36% (Brazil)
- longer duration
- Peripheral neuropathy



Vitamin E supplementation

↓ HOMA-IR, HbA1c, Insulin
Short-term: ↓ FBS
Long-term: lipid profile

Meta-
analyses
of RCTs
(Low
certainty)

400 and 700 mg/d
optimal for HbA1c
and insulin levels
(T1DM)

Dose

DR, DN

600 to 1,800 IU daily
(greater benefit when
co-administered with
vitamin C)
Lack of evidence

Import
ant
points

- Vit E: HDL (simvastatin and niacin)
- ≥ 300 mg: interaction with aspirin, warfarin, cyclosporine, tamoxifen
- High dose: Vit K, W6
- > 400 IU (180 mg): acute stroke, prostate cancer, death (>70 mg)

Asbaghi O, et al. 2023

Jin Z, et al. 2023

Mohammad A, et al. 2021

Zheng PP, et al. 2024

Matough FA, et al. 2012

Emami MR, et al. 2019

Liu I, ET AL. 2020

Ghatziralli. 2017

Shi C, et al. 2020



RDA (E)

Age	Males	Females	Pregnancy	Lactation
0–6 months*	4 mg	4 mg		
7–12 months*	5 mg	5 mg		
1–3 years	6 mg	6 mg		
4–8 years	7 mg	7 mg		
9–13 years	11 mg	11 mg		
14+ years	15 mg	15 mg	15 mg	19 mg

UL (E)

Age	Male	Female	Pregnancy	Lactation
1–3 years	200 mg	200 mg		
4–8 years	300 mg	300 mg		
9–13 years	600 mg	600 mg		
14–18 years	800 mg	800 mg	800 mg	800 mg
19+ years	1,000 mg	1,000 mg	1,000 mg	1,000 mg

To convert from mg to IU:

1 mg of alpha-tocopherol is equivalent to 1.49 IU of the natural form or 2.22 IU of the synthetic form.

To convert from IU to mg:

1 IU of the natural form is equivalent to 0.67 mg of alpha-tocopherol.

1 IU of the synthetic form is equivalent to 0.45 mg of alpha-tocopherol.



Vitamin E

1 tbsp wheat germ oil: 20 mg

30 g sunflower seeds: 7.5 mg

1 tbsp sunflower oil: 5.5 mg

1 tbsp corn oil: 2 mg

1 kiwi: 1.1 mg

1 tomato: 0.7 mg



Practical instructions



- **Nutritional**
 - **women or older**
 - **Other comorbidity or secondary condition:**
(Abetalipoproteinemia 100 to 200 IU/kg/d, Chronic cholestasis 15 to 25 IU/kg/d, Cystic fibrosis 5 to 10 IU/kg/d, Short-bowel syndrome 200 to 3600 IU/d, Isolated vitamin E deficiency 800 to 3600 IU/d)
 - **Serum α -Tocopherol**
 - **diabetic retinopathy (C+E)**
- Supplementation?**

Chromium

Intake

uncertain

Serum

uncertain

Supplement

uncertain



Chen J, et al.2022
Chen S, et al. 2017
Mclver DJ, et al.2015
Trumbo P, et al.2008

The role of chromium in glycemic control

- *The exact biological role of chromium in humans remains incompletely understood
- *Enhance insulin receptor kinase activity and insulin signaling
- *Increase cellular glucose uptake through enhanced GLUT4 translocation
- *Chromium has been proposed to enhance insulin signaling through a putative chromium-binding peptide (chromodulin), although its physiological existence and function remain controversial.
- *Reduce systemic inflammation ($\downarrow$ CRP, $\downarrow$ TNF- α), particularly in short-term interventions.

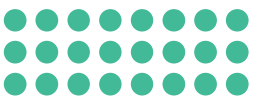
Anderson R.2000

Hua Y, et al.2012

Sheikhhossein F, et al. 2020

Gholami A, et al 2025

Babakr AT, et al 2026



Chromium status



Cr6+



Serum
1-5 $\mu\text{g/L}$
Whole blood
20-30 $\mu\text{g/L}$



Urine
0.2 to 1.8 $\mu\text{g/L}$



Chromium deficiency in diabetes



*Chromium deficiency has not been demonstrated in healthy individuals consuming a typical oral diet.

*Reliable biomarkers and validated cutoffs for chromium status are lacking.

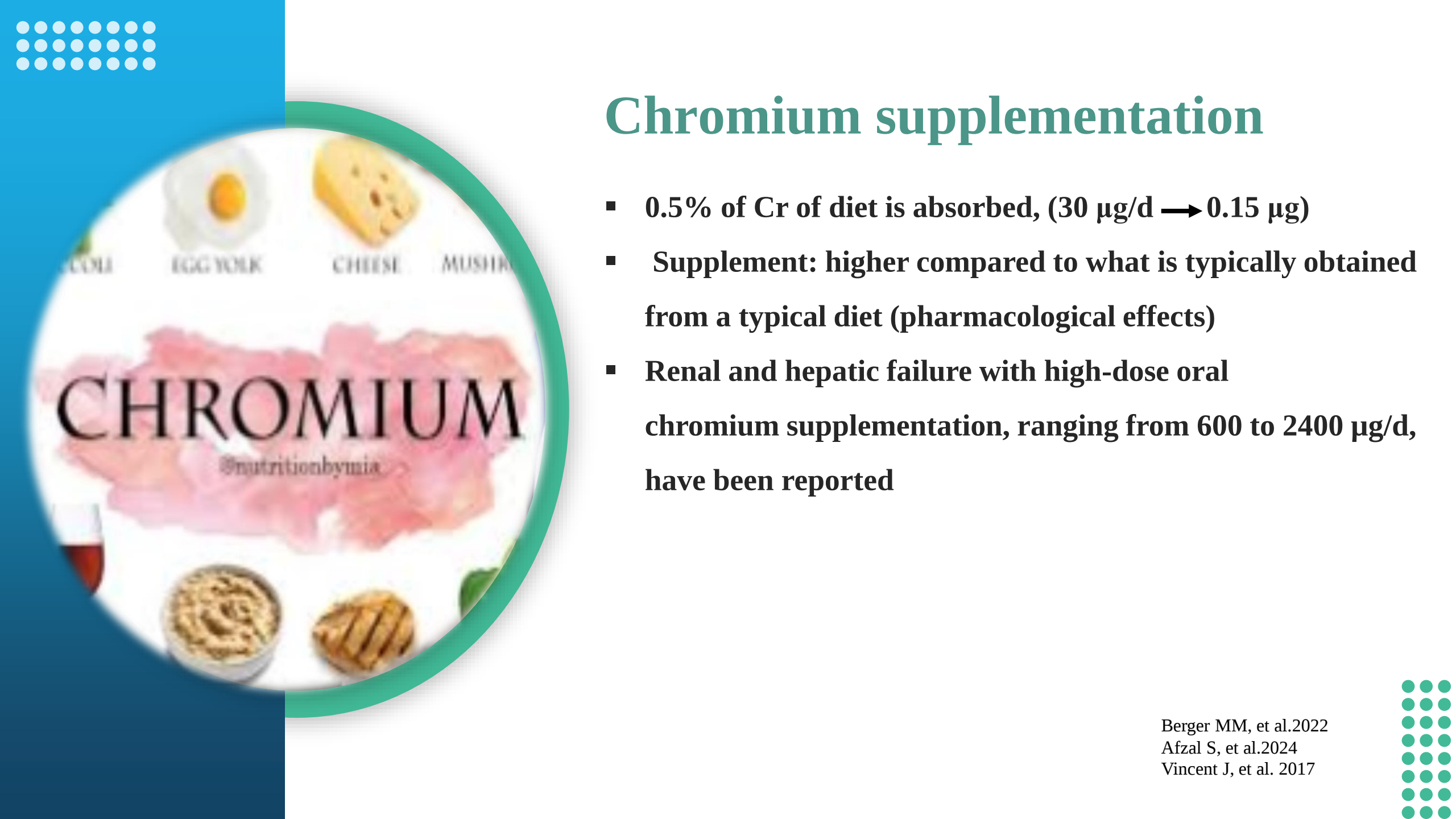
*Reported cases of suspected deficiency mainly involve long-term parenteral nutrition, particularly in patients with intestinal failure or massive bowel resection.

Chromium supplementation

↓ Fasting plasma glucose
↓ HbA1c
↓ Insulin / HOMA-IR
Improvement in TG and HDL-C



Georgaki MN, et al.2024
Asbaghi O, et al. 2020
Suksomboon N, et al. 2014
Asbaghi O, et al.2021
Zhao F, et al. 2022
Ebenuwa I, et al. 2024
Alkhalidi F, et al. 2024
Tirona M, et al. 2023
Berger MM, et al.2022
Afzal S, et al.2024



Chromium supplementation

- 0.5% of Cr of diet is absorbed, ($30\text{ }\mu\text{g/d} \rightarrow 0.15\text{ }\mu\text{g}$)
- Supplement: higher compared to what is typically obtained from a typical diet (pharmacological effects)
- Renal and hepatic failure with high-dose oral chromium supplementation, ranging from 600 to 2400 $\mu\text{g/d}$, have been reported



AI (Cr)

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months*	0.2 mcg	0.2 mcg		
7–12 months*	5.5 mcg	5.5 mcg		
1–3 years	11 mcg	11 mcg		
4–8 years	15 mcg	15 mcg		
9–13 years	25 mcg	21 mcg		
14–18 years	35 mcg	24 mcg	29 mcg	44 mcg
19–50 years	35 mcg	25 mcg	30 mcg	45 mcg
51+ years	30 mcg	20 mcg		

Practical instructions



- **Routine monitoring is not recommended**
- **Nutritional:** Varied diet, Vitamin C increases the absorption of chromium.
- **Deficiency is suspected:** glucose tolerance testing before and after chromium administration
- **Routine supplementation: not recommended**
- + Metformin/ insulin: Hypoglycemia
- Levothyroxine: 6 hours

Zinc

Intake

- High VS Low : ↓13 % risk of DM
- A moderately higher than DRI: ↓13-41%
- Possible U-shaped association with T2DM risk

Serum

- High VS Low : ↑64% risk of DM

Supplement

- No effect (lack of evidence)



Fernandez-caio J. et al. 2019
Dib RE, et al. 2015
Pompano ML, et al. 2021
Shi C, et al. 2020
He P, et al. 2022
Yang J, et al. 2024

The role of zinc in glycemic control

01

Synthesis, storage, secretion, action of insulin

02

Facilitation of insulin signaling and GLUT4 translocation

03

Altered expression of ZnT/ZIP zinc transporters has been reported in T2DM, suggesting cellular zinc dyshomeostasis

Zinc status based on plasma concentration



Saturated
 $\geq 120 \mu\text{g/dl}$
Toxicity
 ≥ 160



Adequate
 $\geq 70-120 \mu\text{g/dl}$



insufficient
 $< 70-30 \mu\text{g/dl}$
deficient
 $< 30 \mu\text{g/dl}$

Zinc deficiency in diabetes



- **Diabetics have lower serum Zinc VS healthy people (In Asia no Austria & Italy)**
 - **The duration of diabetes associated with the concentration of zinc in blood, is not explained by a lower of dietary zinc intake. Exception in DM complications (nephropathy) (3mg/dl)**
- Prevalence of deficiency: 30-50 %**

Farooq DM, et al.2020

Takuisso, et al. 2025

Fernandez- Cao JC, et al. 2019

Sanjeevi N, et al. 2018

Klein E, et al. 2025



Urinary zinc excretion

- RDA of Zn: 8-11 mg – 40-20% absorption: 2-3 mg (0.5 mg excreted in urine) in diabetes (urinary excretion ↑)
- Daily intake of Zn in diabetes: ↑

Zinc supplementation

HbA1c ~ ↓ 0.3–0.5%
FBS ~ ↓ 14–23 mg/dL
2h glucose ~ ↓ 34–37 mg/dL
HOMA-IR ~ ↓ 0.5–0.7
Insulin ~ ↓ 0.7–1.8 mU/L
TC ~ ↓ 13–16 mg/dL
LDL-C ~ ↓ 6–11 mg/dL
TG ~ ↓ 13–18 mg/dL
HDL-C ~ ↑ 4 mg/dL
↑ Total antioxidant capacity



Daneshvar M, et al.2024
Nazem MR, et al.2023
Wang X, et al.2019
Heidari M, et al.2023
Nazari M, et al. 2024
Ghaedi K, et al.2024
Klein E, et al. 2025

RDA (Zn)

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months*	2 mg	2 mg		
7–12 months	3 mg	3 mg		
1–3 years	3 mg	3 mg		
4–8 years	5 mg	5 mg		
9–13 years	8 mg	8 mg		
14–18 years	11 mg	9 mg	12 mg	13 mg
19+ years	11 mg	8 mg	11 mg	12 mg

UL (Zn)

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	4 mg	4 mg		
7–12 months	5 mg	5 mg		
1–3 years	7 mg	7 mg		
4–8 years	12 mg	12 mg		
9–13 years	23 mg	23 mg		
14–18 years	34 mg	34 mg	34 mg	34 mg
19+ years	40 mg	40 mg	40 mg	40 mg





Zinc

90g beef: 3-4 mg

30g pumpkin seeds: 2.2 mg

50g cheddar cheese: 1.5 mg

90g fish: 0.5-1 mg

One egg: 0.6 mg

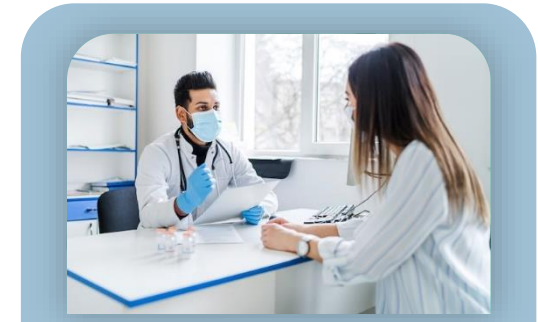
Half a cup of rice: 0.3-0.7 mg

Half a cup of cooked broccoli: 0.4 mg



Practical instructions

- **Duration of diabetes**
- **Other comorbidity or secondary condition: IBD, Celiac, vegan**
- **Nutritional:** lack of meat intake, excess phytates (present in legumes, seeds, soy products, and whole grains), or oxalates (found in spinach, okra, nuts, and tea), Alcohol use disorder.
- Iron supplement ≥ 25 mg elemental iron
- **Thiazide diuretics**
- **Serum zinc** (Checking zinc levels each 3-6 months) (No in Infectious, cachectic, hormone therapy conditions)
- **Supplementation (2-6 h- tetracycline, ciprofloxacin)(1 h- Penicillamine)**
- * **5 mg/QOD elemental zinc**
- * **0.5-1 mg/kg (30 mg/d) elemental zinc, 3-4 month**
- **Serum cu: check, if $< 70 \mu\text{g/dl}$; (For every 30 mg of zinc, 2 mg of copper)**



Thank You

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