Is there a role for selenium in thyroid diseases?

Chairs: A. Frasoldati, F. Monaco

Epidemiology of selenium deficiency	*L. Duntas*
Selenium in the treatment of thyroid diseases	*C. Marcocci*
Take home messages	*A. Frasoldati*

Dietary intake of selenium

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High diversity of selenium status in human populations, worldwide

Mean per day intake: **40 µg - Europe**
93 µg (women), 134 µg (men) - USA

Daily dose recommendations vary in different countries:

- 55 µg/day in the United States,
- 75 µg/day (men) and 60 µg/day (women) UK
- 1 µg/kg/day in France

Doses should not exceed 400 µg/day

Range of Selenium Content in various Foods

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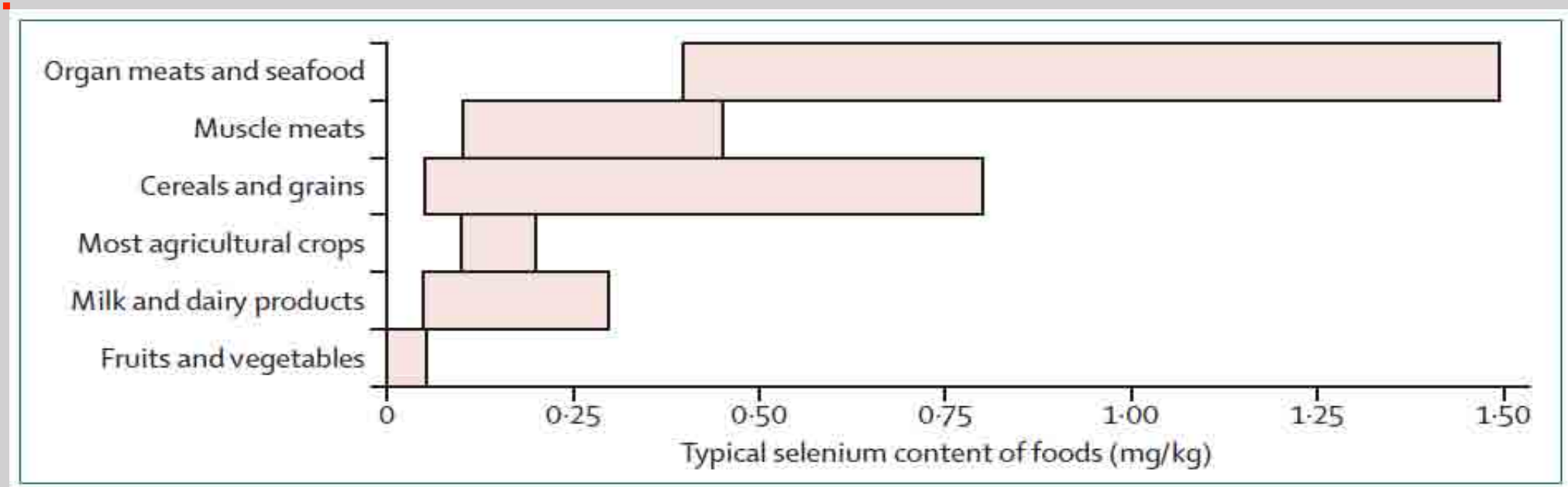

Lancet 2012; 379: 1256–68

Selenium intake: basic figures

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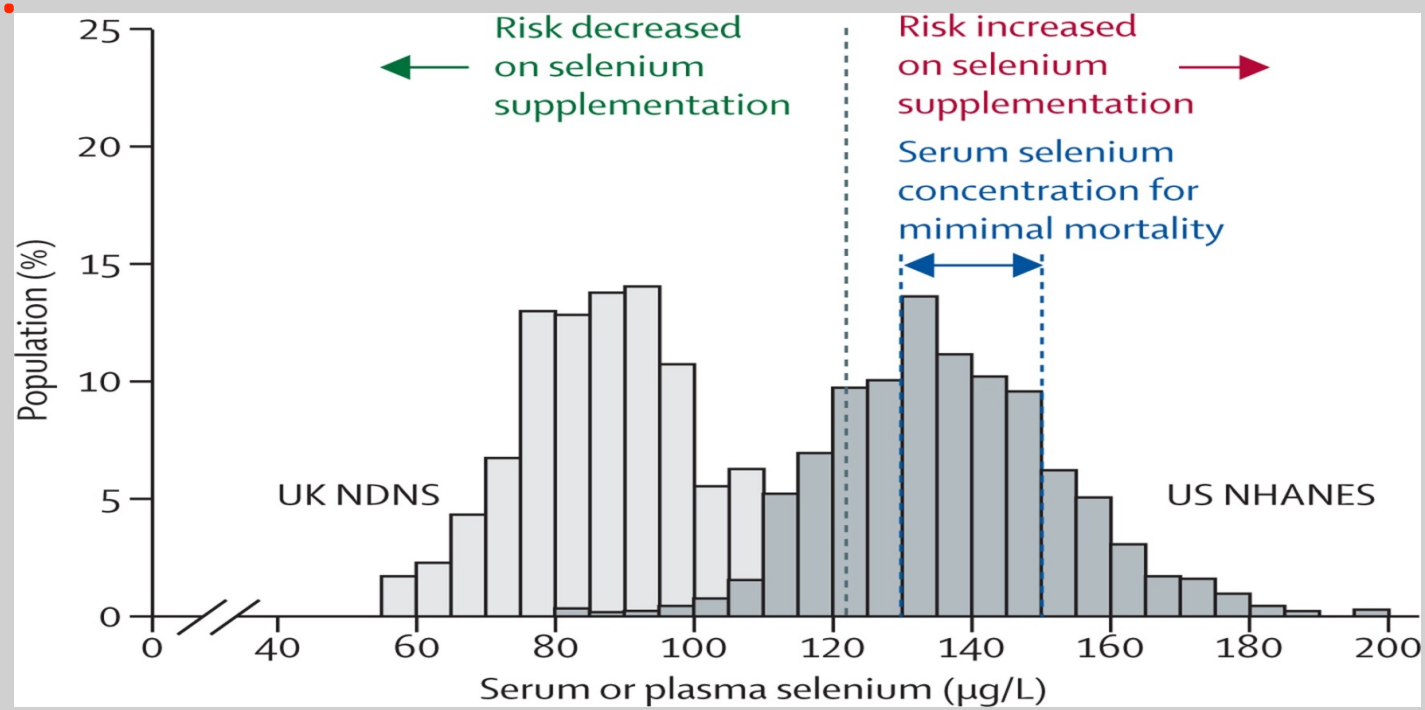
Standard plasma selenium concentrations:

60-120 µg/l (0.8 ± 0.36 µmol/l)

Plasma selenium concentration is related to dietary selenium, whereas selenoprotein P reflects selenium stocks in the body and appears a better marker of selenium status.

Plasma selenium assays not recommended in routine practice

Distribution of serum or plasma selenium in adults



People whose serum or plasma selenium concentration is already 122 µg/L or higher, should not supplement with selenium.

People with serum or plasma selenium concentrations less than 122 µg/L may have benefits from raising their selenium status (e.g. to 130–150 µg/L)

Lancet 2012; 379: 1256–68

Selenium and thyroid nodules

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Prediagnostic serum selenium in a case-control study of thyroid Cancer

European Journal of Endocrinology (2003) 148 309–315

Glattre E, Thomassen Y, Thoresen SO, haldorsen T, Theodorsen L, Aaseth J

Positive association between the incidence of thyroid cancer
And low prediagnostic serum-selenium concentration

Association of selenium with thyroid volume and echostructure in 35- to 60-year-old French adults

Hélène Derumeaux[1], Pierre Valeix[1,2], Katia Castetbon[2], Michel Bensimon[1], Marie-Christine Boutron-Ruault[1], Josiane Arnaud[3] and Serge Hercberg[1,2]

Inverse association between selenium status and thyroid volume, thyroid tissue damage, and goitre in French women

Int J Epidemiol 1989 Mar;18(1):45-9

Selenoproteins implicated in the thyroid function

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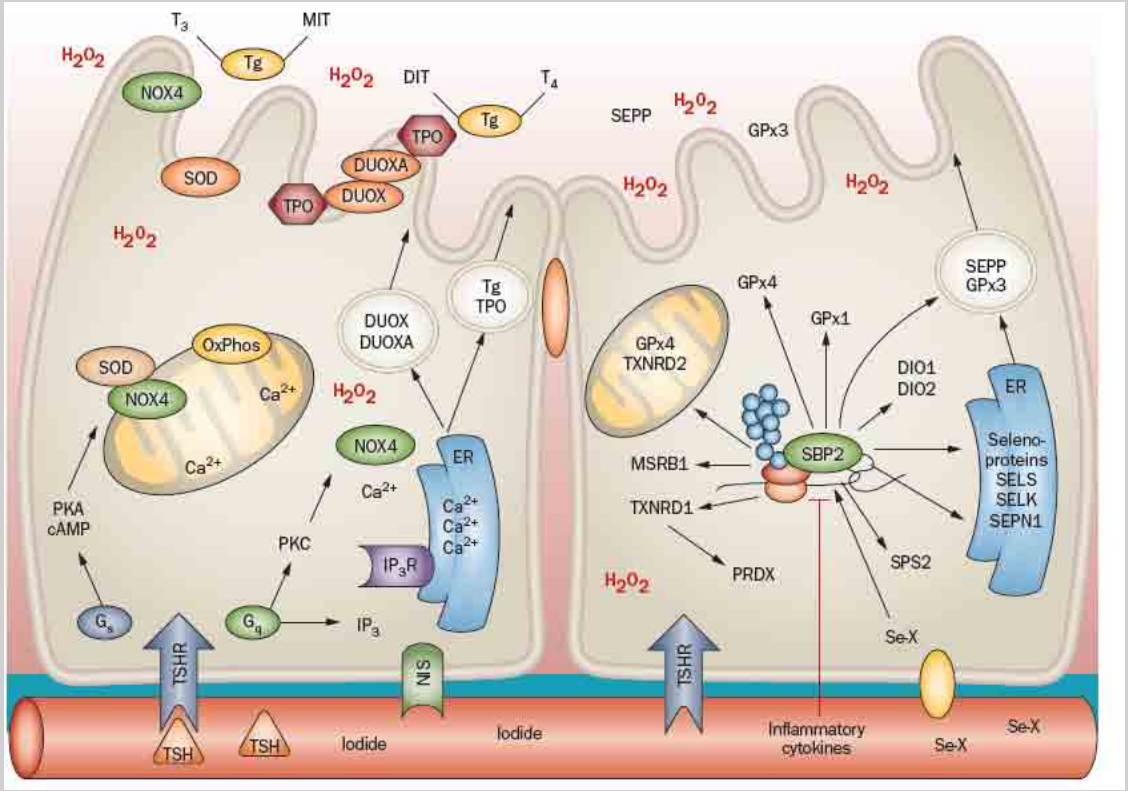

The selenium-dependent iodothyronine deiodinases (DIOs) produce T3 from T4

Selenium, in the form of glutathione peroxidases (GPxs), protects thyroid cells from the hydrogen peroxide generated to be used by thyroid peroxidase in the synthesis of T3 and T4

Endogenous pathways ensure that the thyroid gland and thyroid selenoproteins are exceptionally well supplied with selenium and largely resistant to selenium deficiency

Schomburg, L. (2011) *Nat. Rev. Endocrinol.*

Selenium deficiency and impaired thyroid function:hypothesis

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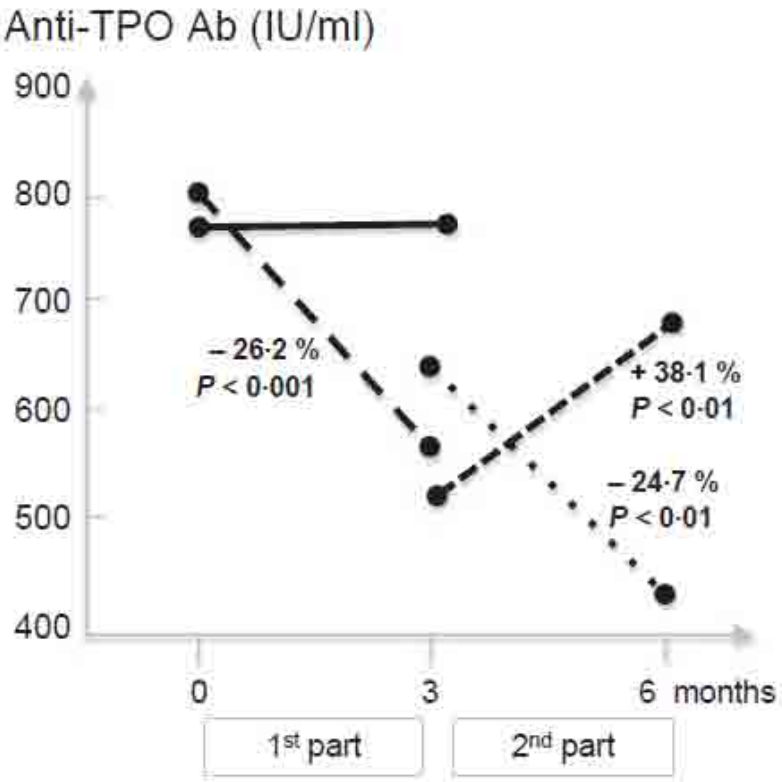
- In selenium-deficiency, sensitive target cells could become insufficiently supplied to allow adequate DIO expression for local thyroid hormone activation and inactivation.
- Intracellular hypothyroid or hyperthyroid metabolic states induced in selenium-sensitive organs by low selenium supply?
- Selenium deficiency likely to constitute a risk factor for a derangement of the immune system–thyroid interaction.

Selenium induces decrease of anti-TPO ab



1st part:

Placebo ($n = 40$)

Selenomethionine 200 µg/day ($n = 48$)

2nd part:

Selenomethionine 200 µg/day ($n = 20$)

Selenomethionine 100 µg/day ($n = 20$)

Turker et al., Journal of Endocrinology, 190, 151–156, 2006

Selenium in autoimmune thyroiditis

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- Selenium supplementation has positive effects in regions of both selenium deficiency and sufficiency, suggesting a pharmacological action in additon to a correction of selenium deficiency

- The lower the selenium levels, the higher the efficacy of treatment

- The higher the amount of anti-TPO, the better the outcome of treatment in terms of reduction of anti-TPO concentration.

Duntas LH, J Clin Endocrinol Metab 95: 5180–5188, 2010

Selenium supplementation in patients with autoimmune thyroid disease

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Table 1 | Outcomes of selenium supplementation studies in patients with Hashimoto thyroiditis

Patients (F/M)	Supplementation regimen	TPOab levels	Country	Reference
70 adults (70/0)	200 μg Na_2SeO_3 per day for 90 days	Decreased by 36%	Germany	150
65 adults (56/9)	200 μg SeMet per day for 6 months	Decreased by 56%	Greece	151
88 adults (88/0)	200 μg SeMet per day for 3 months	Decreased by 26%	Turkey	152
88 adults (88/0)	100 μg SeMet per day for 3 months	No effect	Turkey	152
76 adults (65/11)	80 μg Na_2SeO_3 per day, 1 year	Decreased by 30%	Italy	154
80 adults (80/0)	200 μg SeMet per day for 6 months	Decreased by 11%	Greece	181
36 adults (36/0)	200 μg Na_2SeO_3 per day for 90 days	No effect	Austria	153
253 seniors (NA)	100 μg yeast-derived Se per day for 1 year	No effect	Czech Republic	182
49 juveniles (33/16)	200 μg Na_2SeO_3 per day for 1 year	No effect	Germany	183

The table shows selected treatment regimens, outcomes and patient cohorts. Abbreviations: F, female; M, male; NA, not available; Na_2SeO_3, sodium selenite; SeMet, selenomethionine; TPOab; thyroperoxidase autoantibody.

Schomburg, L*Nat. Rev. Endocrinol.* 2011

Selenium Supplementation in the Treatment of Hashimoto'sThyroiditis

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A Systematic Review and a Meta-analysis

Selenium supplementation is associated with a significant decrease in TPOab titers at 3 months and with improvement in mood and/or general well-being.

Evidence suggests a different pattern of response to Selenium supplementation in HT relative to baseline TPOab titers, and this, if confirmed, could be used to identify which patients would benefit most from treatment.

An improvement in thyroid function and morphology should be demonstrated before Se routine supplementation can be recommended in the treatment of HT.

Toulis KA, Thyroid 20: 1163-1173, 2010

Selenium in autoimmune thyroiditis

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Clinical outcomes should be demonstrated before selenium supplementation can be routinely recommended:

- **reducing the progression rate from euthyroidism to subclinical hypothyroidism**
- **reducing the progression rate from subclinical to overt hypothyroidism**
- **reducing the need of thyroxine treatment**

Toulis KA, Thyroid 20: 1163-1173, 2010

CLINICAL PRACTICE GUIDELINES FOR HYPOTHYROIDISM IN ADULTS

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Selenium has notable theoretical potential for salutary effects on hypothyroidism and thyroid autoimmunity including Graves' eye disease, both as a preventive measure and as a treatment.

However, there are simply not enough outcome data to suggest a role at the present time for routine selenium use to prevent or treat hypothyroidism in any population.

ATA/AACE Guidelines

RECOMMENDATION 33
Selenium should not be used to prevent or treat hypothyroidism.
Grade B, BEL 2

ENDOCRINE PRACTICE Vol 18 No. 6 November/December 2012

Selenium supplementation for Hashimoto's thyroiditis

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The results of this review demonstrate that at present, objective evidence is insufficient to support clinical decision making regarding the use of selenium supplementation for the treatment of patients with Hashimoto's thyroiditis

THE COCHRANE COLLABORATION®

van Zuuren EJ, Albusta AY, Fedorowicz Z, Carter B, Pijl H

Cochrane Library 2013, Issue 6

Selenium and Graves' ophtalmopathy

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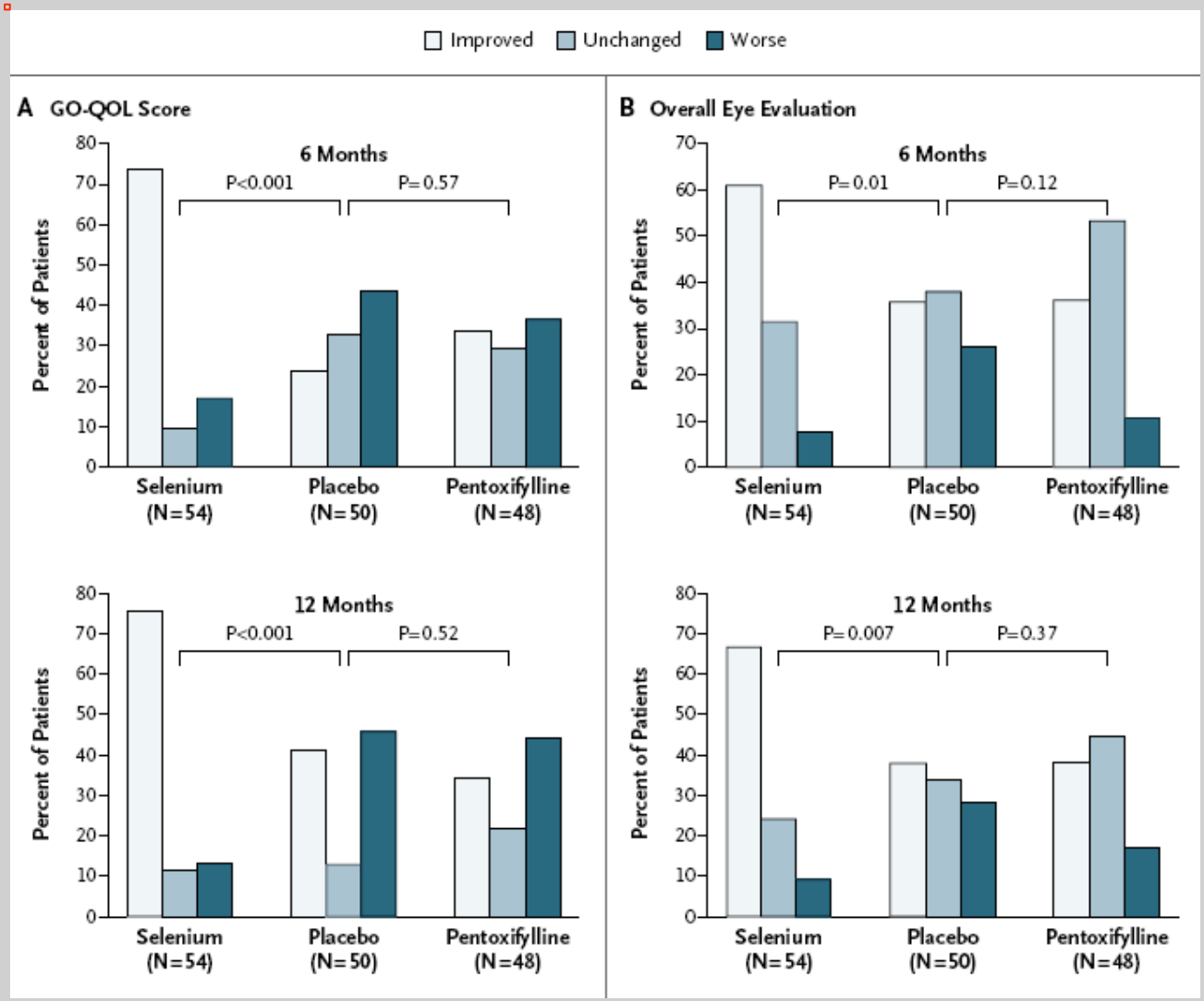
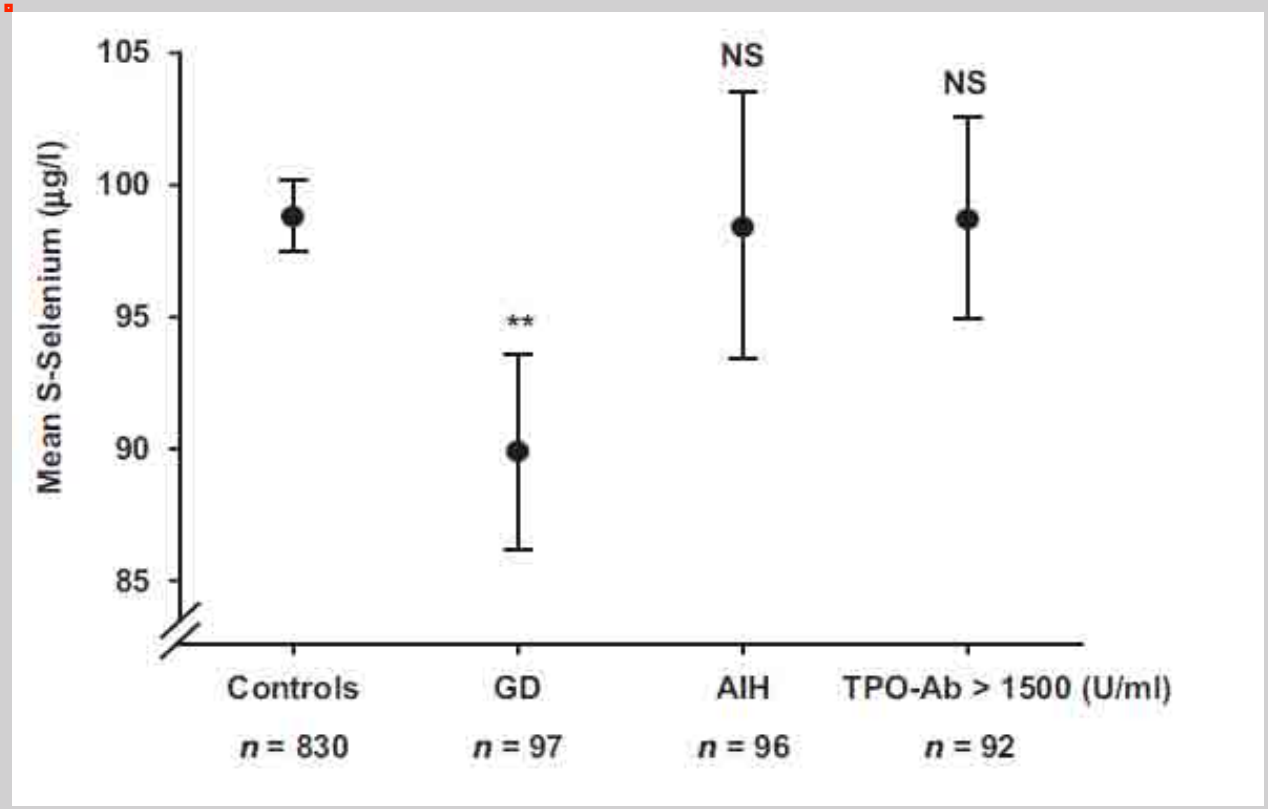


Selenium supplementation (6 months) improves the course of GO and the related impairment in quality of life

Marcocci C et al., N Engl J Med 364:1920-31, 2011

Serum selenium is low in newly diagnosed Graves' disease



Patients with newly diagnosed GD had significantly lower serum Selenium levels compared with random controls.

This observation supports a link between inadequate selenium supply and overt autoimmune thyroid disease, especially GD.

Bülow Pedersen et al., Clinical Endocrinology, 79; pages 584-590, 2013

STUDY PROTOCOL Open Access

Selenium supplementation for patients with Graves' hyperthyroidism (the GRASS trial): study protocol for a randomized controlled trial

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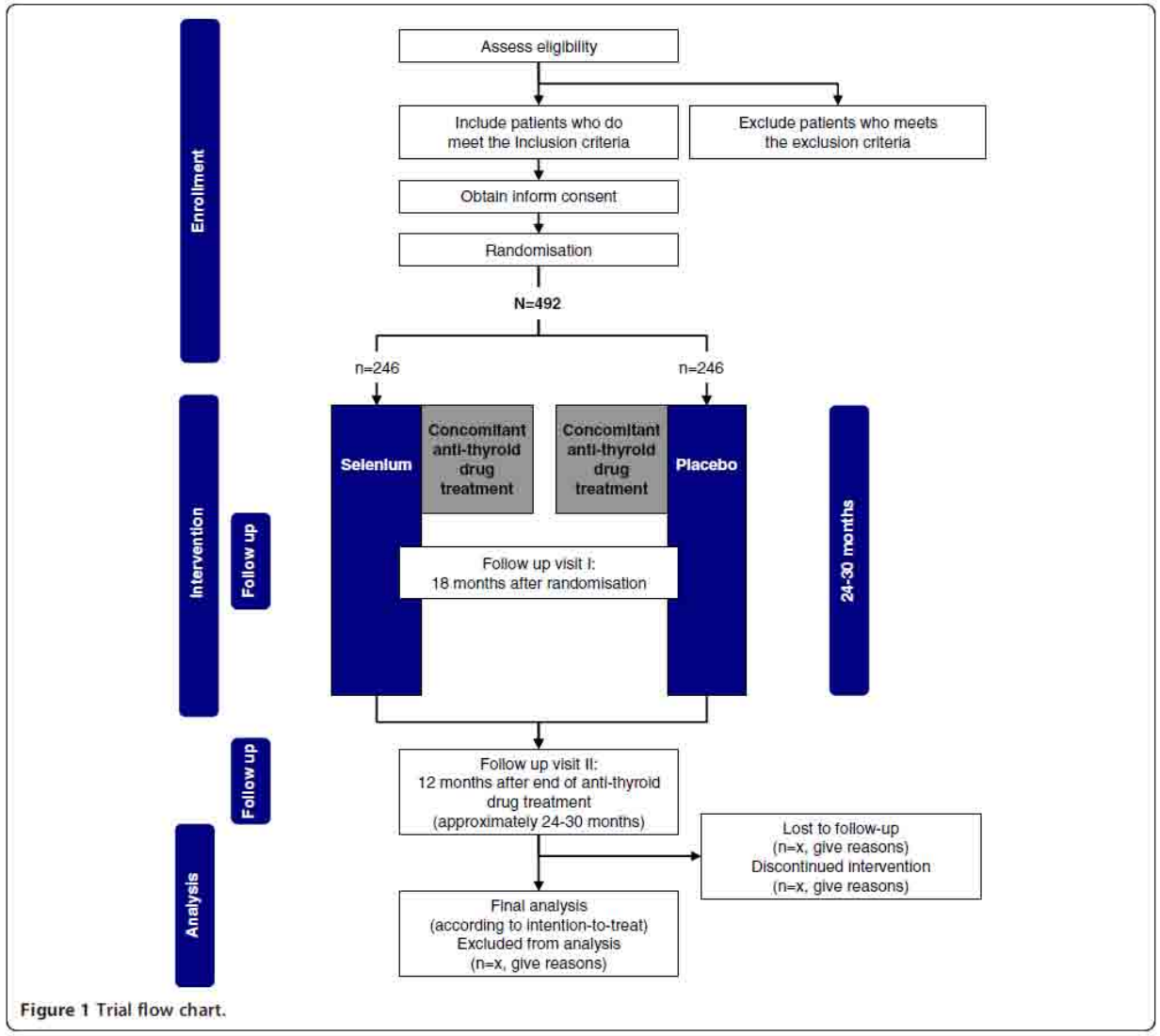

Figure 1 Trial flow chart.

Primary outcome: proportion of participants with anti-thyroid drug treatment failure at the end of the intervention period (24 to 30 months).

Secondary outcomes are:
-thyroid-specific QoL life during the first year after randomisation;
- level of TSHR ab at 18 months after randomisation and at the end of the intervention period (24 to 30 months;
- eye symptoms during the first year after randomisation, and at the end of the intervention period (24 to 30 months

BioMed Central

Watt et al. Trials 2013, 14:119

Selenium in pregnancy

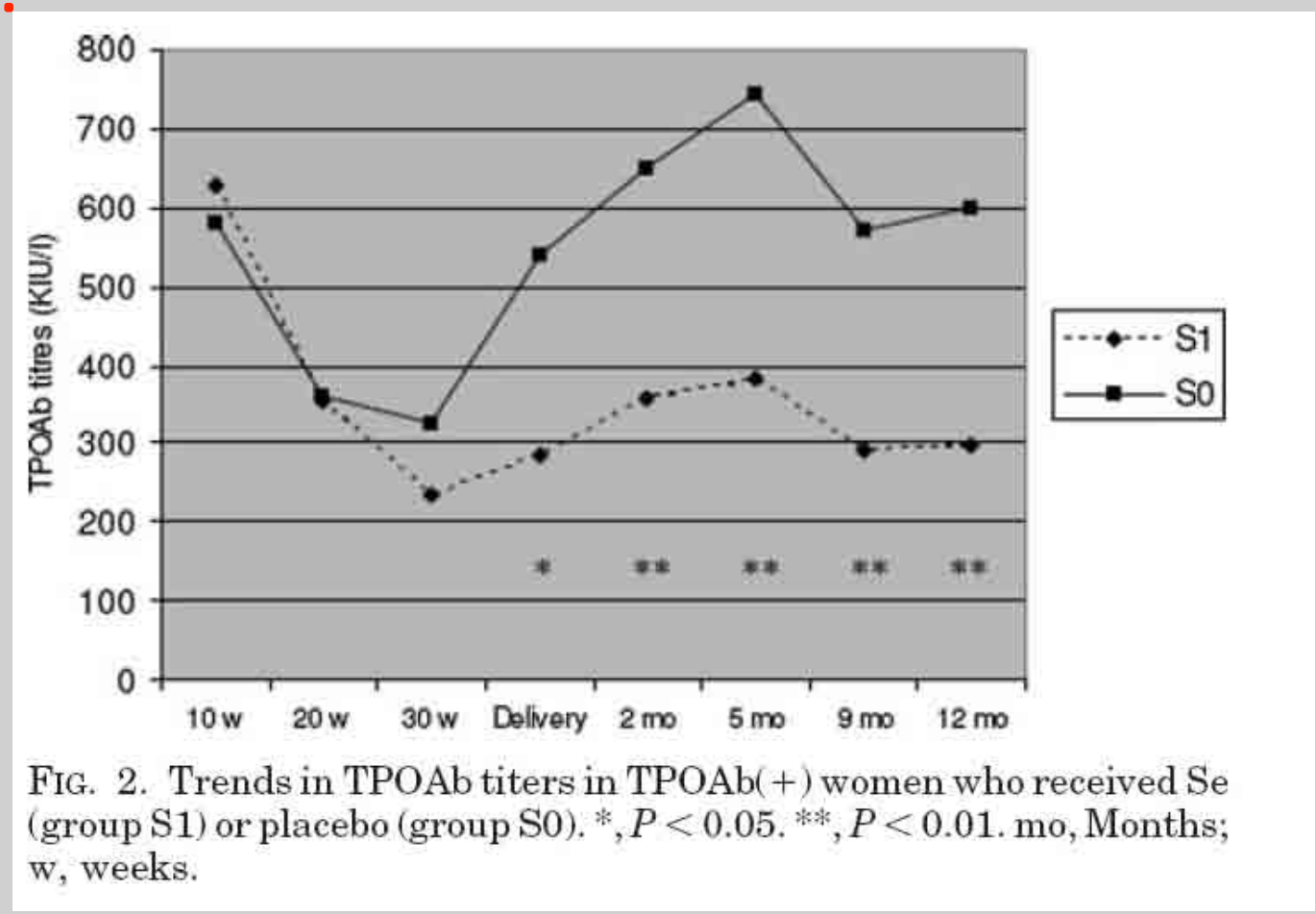

FIG. 2. Trends in TPOAb titers in TPOAb(+) women who received Se (group S1) or placebo (group S0). *, $P < 0.05$. **, $P < 0.01$. mo, Months; w, weeks.

Protective effects by selenium on postpartum thyroiditis and permanent hypothyroidism

Negro R et al., J Clin Endocrinol Metab 92: 1263–1268, 2007

Selenium and the thyroid gland: more good news for clinicians

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- Currently, progression of Hashimoto's disease cannot be avoided but levothyroxine treatment is perfectly tolerated and inexpensive.

- Selenium supplementation can only be considered as an option and justified if it truly improves the quality of life of patients stopping or slowing down thyroid destruction.

- The expected benefits of selenium supplementation appear to be superior in indications such as Graves' disease or Graves' orbitopathy as current treatment options for these disorders are sometimes ineffective, insufficient or poorly tolerated.

Drutel et al., Clinical Endocrinology (2013) 78, 155–164

THM: conclusive remarks 1.

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Selenium is likely to exert multiple effects on human health: further researches are needed to clarify all the possible benefits of its supplementation

Future trials should take into account selenium status and accurate genotyping of participants as polymorphisms in selenoproteins may affect selenium status.

THM: conclusive remarks 2.

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Thyroid function

Selenium administration does not cause changes in free or total T4/T3 levels.

Thyroid nodules/cancer

Selenium status has been inversely correlated to thyroid volume and the prevalence of nodular diseases. Some evidence suggest a relationship between selenium deficiency and thyroid cancer but more studies are needes.

Thyroid autoimmunity

Many, yet not all, studies showed that selenium supplementation (80 µg or 200 µg per day) decreases the TPO ab titre in chronic autoimmune thyroiditis. In Graves' disease, selenium treatment is associated with improved quality of life, reduced eye involvement, and slower progression of orbitopathy.

Is there a role for selenium in thyroid diseases?

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- Mild Graves' ophtalmopathy (GO)

- Autoimmune thyroiditis with high TPOab titer and subclinical hypothyroidism
- Pregnancy TPO+

- Graves'disease without GO
- Severe thyroid autoimmune inflammation

Is there a role for selenium in thyroid diseases?

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