Effects of nutritional supplements on health

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A diet containing all of the 50 essential nutrients in a balanced and need-related ratio may well be the most important pillar of our health. This means that we cannot be content with supplying them at the low marginal level of minimum needs, but should instead aim to ensure an optimum amount of micronutrients etc. every day, if possible. In all age groups, and more often than is generally known, personal performance deficits, also those of the body's own defense against infection and disease, are the result of nutritional deficits, e.g. in nutrient density or the supply of individual dietary components.

A diet modified by the supplementation of missing vitamins and minerals may mitigate or even prevent syndromes of different genesis especially in the case of distress caused by endogenous and/or exogenous factors (stress of all kinds in professional or private situations), and offers the best possible conditions for strengthening the immune system and keeping it active – i.e. protecting good health, which is becoming more and more important in view of rising life expectancy and constantly growing health costs (5, 6, 16, 20, 21, 29).

Summary

Objectives: *Following the supplementation of a number of micronutrients over four months during the winter of 2002/03, we examined to what extent sick days can be reduced, general quality of life improved, immunological parameters favorably influenced, and nutritionally induced performance deficits of working people compensated. What are the results of a cost-benefit analysis of this nutritional intervention?*
Methods: *Fifty-four workers employed in the retail sector were divided into an intervention group IG (34.6 years) and a control group CG (34.9 years). An analysis of data on the number of sick days in previous years was provided. Over the winter months (Dec. 1– Mar. 31) the IG was supplied daily with a micronutrient beverage containing vitamins, trace elements and phytonutrients. Additionally, health and immunological parameters were measured in this group.*
Results: *When comparing the values taken at t1 and t2 for the IG, the following significant results were obtained ($p \leq 0.01$ and $p \leq 0.001$, respectively): Increase in percent: monocytes 15.3%, T cells 5.3%, T-helper cells 6.9%, T-helper/T-suppressor cells ratio 14.0%, natural killer cells 21.6%, immunoglobulin (Ig)A 6.9%, IgG 6.7%, and overall health-related quality of life (SF-36) 29.6%. Decrease in percent: activated T cells -70.9%, IgM -7.6%, C-reactive protein -56.9%, common colds -48.6%, sick days -75.6%. In contrast to this, the number of sick days in the CG remained unchanged during the trial period.*
Conclusions: *These results show that the regular consumption of nutritional supplements alone in the winter months, when resistance is low, led to a significant improvement in the health and immune status and also to a resultant reduction in sick days. Economically, these preventive measures represent a positive »return on investment in human health« of 1:1.9 which emphasizes the effectiveness and practicability of active health promotion and prevention of sickness.*

Key words
Micronutrients, nutritional supplementation, multinutrient-enriched beverage, immunity, common cold, sick days, health promotion, prevention

In order to identify the effects of nutritional supplements (NS) on human health, the following questions were to be answered in a field experiment performed by the Department of Ergonomics at Munich Technical University under the guidance of Prof. Dr. med. Dr. Ing. habil. Wilfried Diebschlag (33) in the winter of 2002/2003: To what extent can sick days (often caused by common colds) be reduced, quality of life/well-being improved, immunological parameters influenced and nutrition-induced performance deficits of working people compensated by a 4-month micronutrient supplementation (vitamins, trace elements, phytonutrients)? What are the results of a cost-benefit analysis of this nutritional intervention?

Methods

Cohort

After preparatory meetings with the partners of the field trial in the retail sector, 54 voluntary subjects of average working age who had submitted their written consent were randomly divided into two equal groups, i.e. an intervention group (IG) and a control group (CG). The total average age of the 17 female and 10 male subjects in the intervention group was 34.6 ± 9.3 years. The age and gender distribution in the CG (34.9 ± 10.9 years, 18 females and 9 males) could be made to match the IG to a large extent. Thus, when comparing the two groups IG vs. CG with regard to sick days, age and gender biases could be excluded.

Intervention measures

Over the winter months (Dec. 1– Mar. 31), the IG took daily, also on weekends,

a micronutrient granular powder (Orthomol® Immun) dissolved in either water or fruit juice as a beverage distributed throughout the day (composition see Table 1). The CG retained its usual dietary habits and lifestyle and did the same work as the IG. For cost reasons placebo powder beverages could not be used, and performing this trial as a double-blind study was impossible for the same reason.

Examination methods

In a medical practice, a team of investigators (an occupational physician, a general practitioner, and a nutritionist) examined various health and immunological parameters of the subjects using the following measuring methods:

- Baseline and final questionnaire (21): sociodemographic data, eating/drinking habits, sports/leisure time activities, physical work load, state of health/complaints, etc.
- Blood pressure and heart rate at rest
- Blood analysis (50): complete blood count, lymphocyte subpopulations, immunoglobulins (Ig), C-reactive protein (CRP), total protein
- SF-36 health survey questionnaire (12)
- Sick day analysis
- Cost-benefit analysis

Table 1: Supplemented micronutrients in the Intervention Group per day compared with the D-A-CH (German – Austrian – Swiss) Dietary reference intakes (DRIs). (19)

Nutrients	Supplementation	DRI per day**	
Vitamins		**Women**	**Men**
Vitamin A (mg Retinol Equivalent)	0,75	0.8	1.0
Vitamin D_3 (µg)	5	5	
Vitamin E (mg) (TE***)	150	12*	14*
Vitamin K (µg)	60	60*	70*
Vitamin B_1 (Thiamine) (mg)	25	1.0	1.2
Vitamin B_2 (Riboflavin) (mg)	25	1.2	1.4
Nicotinamide (mg)	60	13	16
Pantothenic Acid (mg)	18	6*	
Vitamin B_6 (mg)	25	1.2	1.5
Folic Acid (µg Folate Equivalent)	800	400	
Vitamin B_{12} (µg)	6	3	
Biotin (µg)	225	30–60*	
Vitamin C (mg)	950	100	
Trace Elements		**Women**	**Men**
Iron (mg)	8	15	10
Iodine (µg)	150	200	
Zinc (mg)	10	7	10
Selenium (µg)	50	30–70*	
Copper (mg)	0.5	1.0–1.5*	
Manganese (mg)	2	2–5*	
Chromium (µg)	30	30–100*	
Molybdenum (µg)	60	50–100*	
Phytonutrients			
Citrus Bioflavonoids (mg)	5	-	
Mixed Carotenoids (mg) (incl. beta-carotene, lutein, lycopene, etc.)	5	beta-carotene: 2–4*	

* Estimated values for an adequate daily supply
** The nutrient recommendations are for healthy people (examples are given here for the 25–51 year-old age group) and only take into consideration conditions that generally lead to increased needs, e.g. pregnancy, breast feeding, and growth.
*** Tocopherol Equivalent

The various parameters of the test battery were measured at both time points, i.e. t1 (baseline examination before intervention, Nov. 30, 2002) and t2 (final examination after intervention, Apr. 1, 2003) in all subjects under uniform, standardized conditions.

Statistics

The measured data were statistically evaluated by means of the statistical software package SPSS, version 11.5. The data were first checked for standard distribution using the Kolmogorov-Smirnov test. As the data had standard distribution, the results for all trial categories of baseline (t1) and final (t2) values were expressed as mean values (M) with standard deviation (SD) and checked for significant changes by means of the parametric t-test for dependent samples from the IG and CG. The usual significance level with an error probability of $p \leq 0.05$ (significant, *), $p \leq 0.01$ (very significant, **), and $p \leq 0.001$ (highly significant, ***) was applied.

Results

At t1, most subjects in the study population did not meet the minimum requirements of health-preserving nutrition: the consumption of vegetables, salads, fruit, whole-grain cereal products/potatoes, as well as milk and dairy products rich in vitamins, minerals, phytonutrients and fiber, was definitely too low from a nutritional point of view with regard to both the frequency of consumption on weekdays and especially the number of subjects. Thus, only 3.7% and 22.2% respectively ate fresh vegetables/salads and fruits daily or several times a day. Instead of the extremely low daily con-

sumption of whole-grain cereal products of only 7.4%, the subjects preferred white flour products with a low nutritional value. Almost all subjects said they ate potatoes ≤ 3 times per week. Meat and sausage products as well as chocolate and cocoa products, whose consumption is less desirable due to their relatively high fat and sugar content, were eaten ≥ 5 times per week by half of the subjects interviewed. These eating habits confirm the data of the "Nutrition Report 2004" by the German Nutrition Society (DGE – Deutsche Gesellschaft für Ernährung) according to which most Germans eat unhealthily ("too much, too rich, too sweet") (18).

Table 2: Selected immunological blood parameters at t1 and t2

Immunological blood parameters	Intervention Group (n1 = 27)			Reference range
	t1 M (± SD)	t2 M (± SD)	Difference (%)	
Monocytes (%)	6.88 (2.18)	7.93** (1.96)	+1.05 (15.3%)	2-14
T cells (%)	70.32 (7.89)	74.02** (9.12)	+3.70 (5.3%)	59-85
Activated T cells (%)	7.55 (5.59)	2.20** (1.69)	-5.35 (70.9%)	-10
Helper T cells (%)	45.16 (7.22)	48.27** (9.04)	+3.11 (6.9%)	29-61
CD4/CD8 ratio	2.15 (0.85)	2.45*** (1.08)	+0.30 (14.0%)	0.9-3.6
Natural killer cells (%)	13.12 (6.78)	15.96** (8.05)	+2.84 (21.6%)	5-25
IgA (mg/dl)	174.04 (65.32)	186.11*** (65.69)	+12.07 (6.9%)	70-400
IgG (mg/dl)	957.11 (179.76)	1021.30** (242.66)	+64.19 (6.7%)	700-1600
IgM (mg/dl)	112.44 (52.07)	103.85*** (50.39)	-8.59 (7.6%)	40-230
C-reactive protein (mg/l)	3.43 (3.04)	1.48*** (1.27)	-1.95 (56.9%)	<5

Probability of error in the t-test for dependent samples
* p ≤ 0.05; ** p ≤ 0.01; *** p ≤ 0.001 (two-sided test)

Blood pressure and heart rate

The systolic as well as the diastolic blood pressure at rest dropped in the IG between t1 and t2 by 8.2% which is highly significant (from 126.1 ± 14.0 to 115.7 ± 12.8 mmHg) and 9.5% (from 80.2 ± 10.0 to 72.6 ± 10.7 mmHg), respectively. At the same time, a very significant 9.0% reduction in the heart rate at rest was observed (from 73.6 ± 7.7 to 67.0 ± 8.9 beats/min), which means that at rest the number of heart beats in 24 hours was 9504 lower than it had been at the beginning of the trial (11, 38).

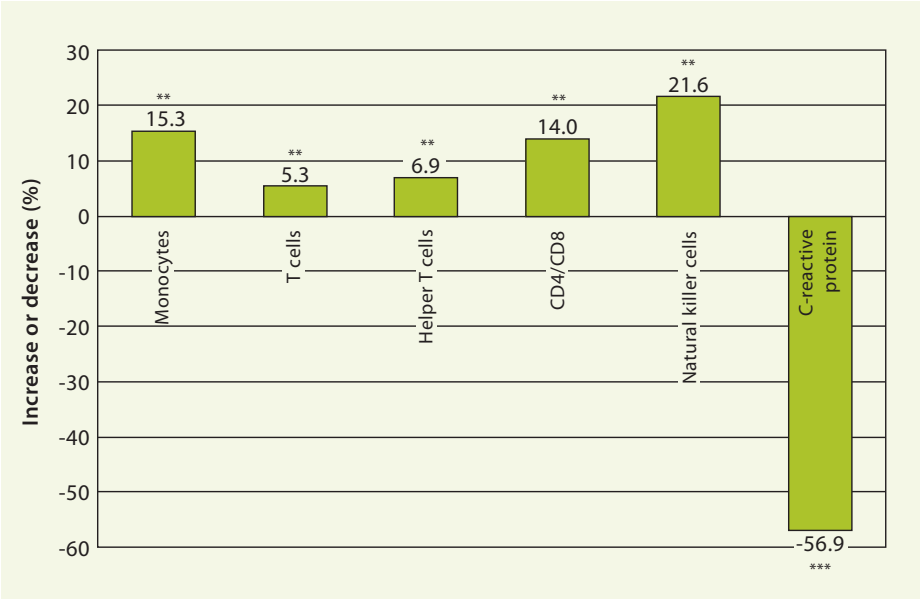

Fig. 1: Increase or decrease (in percent) of significant changes in various immune parameters in the Intervention group (IG) after 4-month micronutrient supplementation

Blood analysis

Table 2 and Fig. 1 show significant changes in certain selected immunological blood parameters after the 4-month micronutrient supplementation. In the IG a very or highly significant increase in monocytes, T cells, T-helper cells, the T-helper/T-suppressor cell (CD4/CD8) ratio, natural killer (NK) cells, IgA and IgG with their many diverse defense functions, and a very to highly significant decrease in activated T cells, IgM and CRP was observed. The subjects' T-suppressor cells dropped by a non-significant 4.0%, whereas the IgE value rose by a non-significant 11.2%. B cells, total protein and several

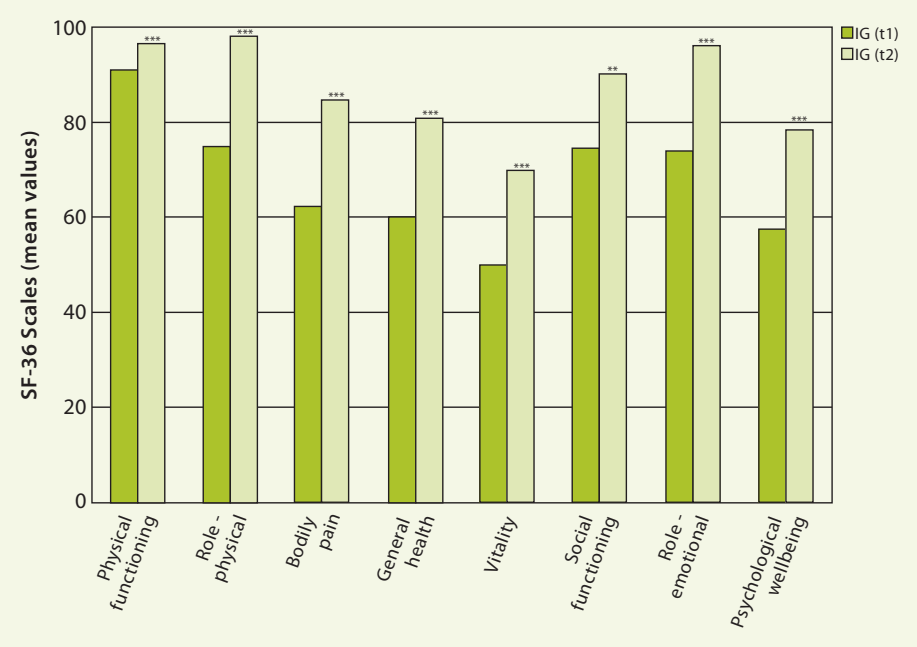

Fig. 2: SF-36 scales (0-100) of the IG when comparing t1 and t2. According to the SF-36 evaluation rules, a higher value indicates a better state of health (for instance, a high value in the Bodily Pain scale means freedom from pain) (12; ** $p \leq 0.01$; *** $p \leq 0.001$)

parameters of the complete blood count remained largely unchanged in the t1 – t2 comparison.

SF-36 health survey questionnaire

The Short-Form-36 questionnaire used, which has become the most frequently internationally used instrument for measuring the subjective state of health and/or health-related quality of life, contains eight scales and an evaluation of the health trend in a total of 36 items (12). As Fig. 2 demonstrates, the t1 – t2 comparison in the IG shows highly significant improvements in the health-related quality of life in almost all scales of the SF-36 (very significant in the Social Functioning scale). Thus, in the Role-Physical, Bodily Pain, General Health, Vitality, Role-Emotional and Mental Health an improvement of ≥ 30.0% was observed. The highest gain of 39.5%, however, was shown in the Vitality scale. Compared with the German standard sample (n = 6964) of the SF-36, the supplemented IG at t2 had considerably better scores in the eight scales (24). The result of the evaluation of the current state of health compared to that of the previous year in the IG is also worth mentioning. The comparison of t1 and t2 shows a highly significant, i.e. 31.7%, improvement in the general state of health.

Health complaints

The extent of the subjective impairment due to general (e.g. sleep disturbance), physical (e.g. neuralgia) and mental-physical (e.g. inner restlessness) complaints was identified by a complaint index which dropped highly significantly by 29.4% in the IG when t1 was compared with t2. Of the eleven complaints studied, which improved without exception, only the results related to colds will be further discussed here. At the start of the trial, 41% of the subjects in the IG suffered from colds frequently to very frequently, and 96% had to deal with recurrent

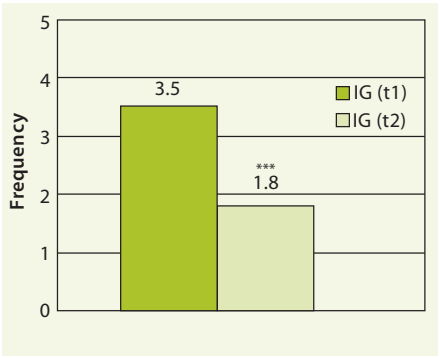

Fig. 3: Occurrence of colds (1 = never to 5 = very often) in the IG when comparing t1 with t2.

colds (occasionally, often, very often). As shown in Fig. 3, the active agents in the beverage given to the subjects led to a highly significant 48.6% reduction in the winter-time colds. Moreover, several IG subjects said that, compared to colds they had in the past, not only the frequency but also the intensity of symptoms had decreased. For this reason, they had been able to go to work as their subjectively perceived symptoms were less severe.

Sick day analysis

In the trial period, a highly significant reduction of 75.6% was also stated in the sick (unfit for work) days in the IG when the previous year was compared with the subsequent one (Table 3). In contrast, the sick days in the CG increased slightly, i.e. 3.8% (not significant). Thus, the comparison of the previous with the subsequent year showed a highly significant decrease in the total sick days by 155, in the CG there was an increase of 7 days. Besides the clearly favorable effect of the supplementation on the number of sick days, it also appears from Fig. 4 that the sick days in the IG in the previous year and the sick days in the CG in the previous and subsequent year were at about the mean level of the

Allgemeine Ortskrankenkassen (local statutory health insurance funds) which was calculated on the basis of the three absence rate reports 2000/2001/2002 (n = 11.7 million) (1, 2, 3).

Cost-benefit analysis

The range of business management methods includes a large number of possibilities for analyzing the efficiency of intervention measures, e.g. a cost-benefit analysis (44). In the field trial described here using a beverage enriched with active agents, the direct plus indirect costs (EUR 19,740 incl. medical examination costs) as well as the benefit (EUR 36,960) were calculated and compared with each other. The result was a positive cost-benefit ratio of 1:1.9.

Discussion

Both occupational physicians and nutritionists are convinced that an exclusively well-balanced diet with ingredients that supplement one another is the goal that should be pursued for the working population and all other individuals.
Unfortunately this is not possible on a long-term basis due to many disturbing factors in everyday working and private lives, and personal negative habits also frequently play a role. Therefore, certain nutrient supplementations appear to be beneficial to health.

Our "sixth sensory organ", the immune system, is a highly developed system with many interconnected mechanisms that protect us against all kinds of pathogens and keep us healthy – ideally as long as we live. We know from various studies made in recent years that an inadequate supply of the micronutrients vitamin A, beta-carotene, folic acid, vitamins B_2, B_6, B_{12}, C, D, E, as well as iron, manganese, copper, selenium and zinc will have a negative effect on immunological parameters. (8, 10, 43).

It was consequently important to review the effect of the daily consumption of a beverage enriched with vitamins, trace elements and phytonutrients on the immune system and the sick days of the working population in the winter months which are stressful to health. In the supplemented IG a very significant increase in the immunocompetent T cells and immunoregulatory T-helper cells as well as in the cytotoxically active monocytes and NK cells with a significantly lower T-cell activation was observed compared with the start of the trial, which indicates a positive correlation between the micronutrient supply and changes in the immunological cell function. At the same time, a highly significant increase in the CD4/CD8 ratio was found, which is considered a benchmark for a rough evaluation of the immune status. Just very recently, scientists in the Netherlands found out that older individuals (n = 436) with a low level of T-helper and NK cells have a significantly higher mortality risk which leads to a very favorable interpretation of our practical and easily realized intervention measure (35).

These results confirm and broaden observations made in previous placebo-controlled studies that report about a

Table 3: Sick days (Dec 1, 2002 – Mar 31, 2003) comparing previous with subsequent year

Sick days	Intervention Group (n1 = 27)			Control Group (n2 = 27)		
	Previous year M (±SD)	Subsequent year M (±SD)	Difference (%)	Previous year M (±SD)	Subsequent year M (±SD)	Difference (%)
Sick days per empoyee	7.59 (4.02)	1.85*** (1.63)	-5.74 (75.6%)	6.78 (3.70)	7.04 (3.63)	+0.26 (3.8%)
Total sick days	205	50	-155	183	190	+7

Probability of error in the t-test for dependent samples
* p ≤ 0.05; ** p ≤ 0.01; *** p ≤ 0.001 (two-sided test)

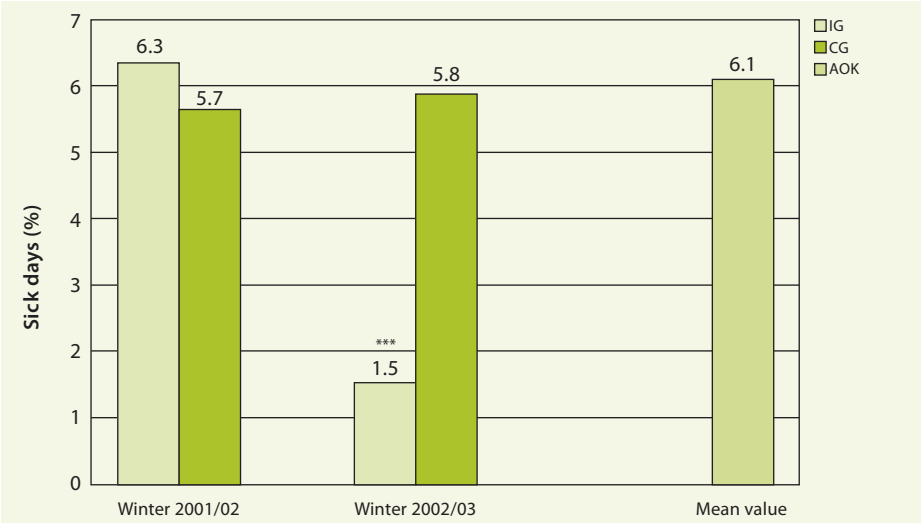

Fig. 4: Sick days (%) (Dec. 1 – Mar. 31) of the IG and CG in the previous vs. subsequent year and in comparison with AOK (Allgemeine Ortskrankenkassen, see above) mean values (n = 11.7 million)

significant lymphocyte stimulation and increase in antibody release in healthy older people when giving them (daily) a multivitamin/multimineral substance. It was also typical in this context that the supplemented groups had on average 50% fewer sick days due to infections/colds in comparison with the placebo groups (4, 13, 15, 36, 41, 42).

An important marker: the C-reactive protein

The highly significant reduction of CRP in the IG by 56.9% has to be particularly emphasized. As the classical acute-phase protein, CRP enables an early diagnosis and evaluation of inflammatory necrotic and neoplastic processes. In a series of epidemiological long-term studies it could also be recently confirmed that a slightly elevated CRP level in healthy individuals indicates an elevated risk of future cardiovascular events. Besides being important as an independent risk marker/predictor, also for the metabolic syndrome and type-2 diabetes mellitus, CRP plays a significant role in the pathogenesis of arteriosclerosis which is also largely independent of other risk factors (39, 40, 45, 50). In a placebo-controlled, double-blind study including 87 subjects (average age 53 years) at the Cooper Institute in Dallas, performed at the same time as our field trial, a 6-month multivitamin supplementation also resulted in a significant reduction of the CRP level compared with the placebo group (17). In two other studies, the one-time administration of vitamin D (n = 171) and/or vitamin C (n = 160) significantly lowered the CRP value by 23% and 24%, respectively (9, 49). In this context it should also be mentioned that in various studies a significant association was found to exist between low concentrations of vitamin A, carotenoids (alpha- and beta-carotene, lutein, cryptoxanthin, zeaxanthin, lycopene), vitamin B_6, vitamin C, vitamin D, vitamin E, iron, selenium and zinc and elevated CRP concentrations (26, 27). In view of the above, the CRP reduction we documented is not an incidental finding.

Improving the quality of life

In addition, the subjects reported a considerable, i.e. 29.6%, gain in the quality of life after completion of the 4-month intervention with micronutrients. With regard to the highly significant strengthening of the subjects' mental balance, it has to be mentioned that neuropsychiatric symptoms including states of depression were mostly associated with an insufficient supply of micronutrients (especially vitamins D, B_1, B_2, B_6, B_{12}, folic acid, biotin, vitamin C, iron, selenium and zinc), and that targeted supplementation can reduce the symptoms (22, 46). In a current study (n = 96), for instance, it was found that taking a multivitamin supplement is associated with a low plasma interleukin-6 level (47), which is considered an independent factor of influence on various depressive symptoms (31, 48). According to another placebo-controlled trial (n = 231), a vitamin-mineral supplementation also has a significantly beneficial influence on "social behavior" (30) – a finding that underlines the very significant improvement in the SF-36 scale of Social Functioning.

As a result of many synergistic interactions and/or protective effects, the combined use of all vitamins whose effectiveness is supplemented by minerals, phytonutrients etc. is sensible in a fixed combination for prevention purposes. Micronutrient supplements, however, must never serve as an excuse for an unhealthy lifestyle and poor eating habits! Instead, they should support and optimize efforts for a healthy lifestyle (5).

Significance for healthcare costs

In summary, it can be stated that in the retail sector where the trial was performed (with dry and dusty air, work mainly done standing up) the administration of micronutrient-enriched beverages led to a highly significant (re)stabilization/improvement of the employees' health and, as a result, to a highly significant reduction in sick days compared with the control group.

Absenteeism due to sickness is always connected with considerable costs for both industry and public administration as well as for the statutory health insurance funds and the national economy as a whole (1). If we consider that the cost of a workday lost due to sickness in the retail sector amounts to a total of approx. EUR 350, the preventive health measure we described above represents a return on investment in human health of 1:1.9. This means that just by optimizing micronutrient supplies, sickness costs amounting to billions can be saved (7). Thus, Prof. Dr. K.W. Lauterbach of the Institute of Health Economics in Cologne has calculated that the German healthcare system would save EUR 4.6 billion every year if an adequate vitamin E supply were ensured. At a time of steadily rising healthcare costs (EUR 240 billion in 2003), an inexpensive, preventative intake of micronutrients on a regular basis thus assumes a dimension in terms of healthcare costs that should not be underestimated besides its purely

medical prevention aspect (14, 32, 37), especially if we consider that, due to the great cost pressure in the healthcare system, more responsibility of the individual for his/her own health and of companies for the health of their employees and the elimination of health disorders is inevitable – self-management is considered the key qualification of the 21st century (23).

The question whether investments in one's own and/or employees' health, i.e. by regularly taking micronutrient supplements, can be cost-efficient in a private, working or economic environment can be responsibly answered in the affirmative without any doubt (15, 21, 22, 36, 51). As the share of staff expenses relating to the total expenses has to be assumed to be as much as 70% in service enterprises, the special importance of intervention measures that promote good health and thus reduce staff costs becomes evident. It should be added in this context that this "caring for one's employees" also has remarkably beneficial psychosocial effects on, for example, the overall quality of life/vitality of the individual and, as a result, on his/her job performance (20).

Acknowledgement

Special thanks are expressed to Prof. Dr. med., Dr.-Ing. habil. Wilfried Diebschlag, manager of the field trial, my teacher of many years and doctoral supervisor, for his untiring scientific and personal support during the 11 months of the study. On February 19, 2004, Professor Diebschlag passed away after a long illness, but still unexpectedly, at the age of 65, in Grafenstein, Austria. Professor Diebschlag's fighting spirit, his ideas and courage will be missed by all who had the privilege of working for him and with him (34).

Statement by the author

The author declares that there is no conflict of interests as defined by the guidelines of the International Committee of Medical Journal Editors.

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Source
Hofmeister M., Auswirkungen von alimentären Ergänzungsmitteln auf die Gesundheit. Ernähr Med 2005;20(3):115–22.

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