Dietary indicators for assessing the adequacy of population zinc intakes

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Abstract

The assessment of dietary zinc intakes is an important component of evaluating the risk of zinc deficiency in populations, and for designing appropriate food-based interventions, including fortification, to improve zinc intakes. The prevalence of inadequate zinc intakes can describe the relative magnitude of the risk of zinc deficiency in the population and identify subpopulations at elevated risk. As a cornerstone to evaluating the adequacy of population zinc intakes globally, a set of internationally appropriate dietary reference intakes must be defined. The World Health Organization/Food and Agriculture Organization/International Atomic Energy Agency (WHO/FAO/IAEA) and the Food and Nutrition Board/US Institute of Medicine (FNB/IOM) have presented estimated average requirements (EAR) for dietary zinc intake, and, more recently, the International Zinc Nutrition Consultative Group (IZiNCG) presented a revised set of recommendations for international use. A prevalence of inadequate zinc intakes greater than 25% is considered to represent an elevated risk of population zinc deficiency. As the requirement estimates are derived from smaller, clinical studies and, for children, most components of the estimates are extrapolated from data for adults, it was desirable to evaluate their internal validity. The estimated physiological requirements for adult men and women appear to adequately predict zinc status as determined by biochemical indicators of status and/or zinc balance. With the use of data from available studies, the reported prevalence of low serum zinc concentration and the estimated prevalence of inadequate zinc intakes predict similar levels of risk of zinc deficiency, particularly among pregnant and nonpregnant women. Conformity between these two indicators is less consistent for children, suggesting that further data and/or direct studies of zinc requirements among children are needed.

Keywords: Deficiency, diet, population, requirements, status, zinc

Introduction

An assessment of the prevalence of inadequate intakes of dietary zinc in a population can provide information on the relative risk of zinc deficiency in a population. Because inadequate dietary intake of zinc is the most likely cause of zinc deficiency, dietary assessment is an important component in evaluating its risk. Dietary assessment of zinc intakes may be used to identify subpopulations that are at elevated risk for zinc deficiency, and to identify dietary patterns that contribute to inadequate zinc intakes. This information will be key in developing appropriate food-based interventions for improved zinc status.

Reference data for dietary zinc requirements are theoretically derived, based on knowledge of zinc absorption and excretion determined from small-scale, controlled, clinical studies. Much information from these types of studies has accumulated in recent years, and the available data and models require review. Also, because the resultant requirements are theoretically derived, the plausibility of dietary zinc requirements to predict the risk of zinc deficiency in a variety of populations needs to be assessed. The objectives of this paper are to review accepted methods and data used to derive both physiological and dietary zinc requirements and recommend the most appropriate reference data for international use, and to provide evidence to support the use of dietary zinc requirements to assess the risk of zinc deficiency in populations.

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Derivation of dietary zinc requirements for assessing the adequacy of population zinc intakes

To evaluate the prevalence of persons in a population who are unlikely to acquire adequate amounts of zinc from the diet to meet physiological needs, it is necessary to compare intakes with established reference data for dietary zinc requirements. For zinc, the components that need to be quantified are summarized in **figure 1**. In the past decade, the World Health Organization/Food and Agriculture Organization/International Atomic Energy Association (WHO/FAO/IAEA) and the Food and Nutrition Board/US Institute of Medicine (FNB/IOM) have convened expert committees to develop estimates of human zinc requirements and to propose the corresponding dietary intakes that are needed to satisfy these requirements [1–3]. In 2004, the International Zinc Nutrition Consultative Group (IZiNCG) presented a critical review of the specific data and models used by these committees to derive the estimates [4]. The details of this review and its recommendations for internationally appropriate dietary zinc requirements are presented in the following sections.

Physiological requirements for absorbed zinc

For most age and physiological groups, a factorial method has been used to estimate zinc requirements. The average physiological zinc requirement is the amount of zinc that must be absorbed to offset the amount of endogenous (body) zinc lost from all intestinal and nonintestinal sites. Nonintestinal sources of zinc loss considered include urine, "surface losses" (desquamated skin, hair, nails, sweat), and, in adolescents and adults, semen or menstrual flow. Additional requirements include the amount of zinc retained in accrued tissue in growing children and pregnant women, and the zinc transferred in breastmilk in lactating women. Estimates for zinc requirements derived from all of the above sources are described in detail below.

Adult men

Urinary losses. For adult men, the FNB/IOM estimated the mean urinary zinc excretion to be 0.63 mg/day, based on the amounts reported from 17 previously published studies of individuals whose zinc intakes (4 to 25 mg/day) were within the range at which urinary concentrations are not influenced by zinc intake [1]. The corresponding figure published by WHO (0.3 mg/day) was based on just two studies [5, 6] in men with very low zinc intakes (0.8 to 3.6 mg/day); their urinary zinc losses were then increased by 40% to account for the reduction in urinary zinc excretion due to the very low zinc intakes. IZiNCG [4] concluded that the information derived by the FNB/IOM committee is more reliable because that report included a larger number of studies and only those in which zinc intakes were in the range in which urinary excretion is constant and likely to include the true physiological requirement.

Surface losses. The FNB/IOM report considered just one study of integumental and sweat losses of zinc [7] carried out in 11 adult men whose mean zinc losses of 0.54 mg/day did not change in response to different levels of dietary zinc intakes (range, 1.4 to 10.3 mg/day) during periods of 28 to 35 days. The WHO committees used an earlier study of eight adult men [5] whose surface zinc losses declined from 0.49 mg/day when ingesting 8.3 mg dietary zinc/day, to 0.28 mg/day with 3.6 mg dietary zinc/day. IZiNCG concluded that although surface losses of zinc may decline with very restricted zinc intakes, it is preferable to estimate surface losses when intakes are sufficient to meet physiological needs and therefore used the same data as the FNB/IOM [7]. However, IZiNCG expressed this loss on a per kg body weight basis (i.e., 6.5 μg/kg), as discussed in further detail below.

Semen losses. The FNB/IOM committee considered information from two papers [7, 8] on the zinc concentration of semen and ejaculate volume of 11 men. Semen zinc concentration (0.11 mg/mL) did not change with restricted dietary zinc intakes, and the ejaculate volume decreased significantly only at the lowest level

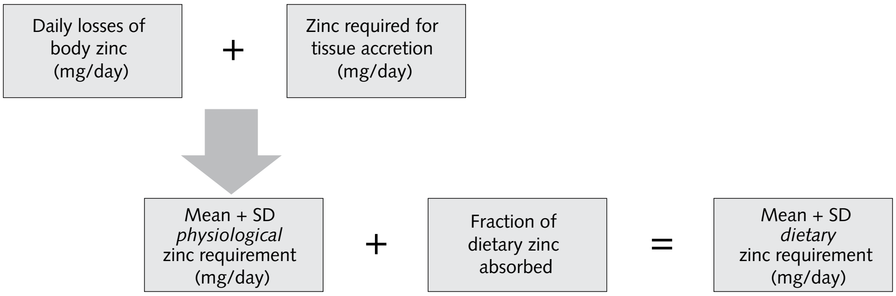

FIG. 1. Information used to estimate dietary zinc requirements

of zinc intake (1.4 mg/day). Thus, the FNB/IOM committee used a single figure of 0.10 mg zinc loss per day in semen, considering a mean ejaculate volume of 2.8 ml and a mean number of 2.45 ejaculations per week. The WHO committees did not include an estimate of zinc loss in semen. Although more information is needed, IZiNCG agreed with the estimates used by FNB/IOM and applied the same figure of 0.10 mg/day.

Intestinal losses. To estimate the intestinal loss of endogenous zinc, the WHO committees used the results from one study reporting a total fecal zinc excretion of 0.5 mg/day in six men receiving 0.28 mg zinc per day for 4 to 9 weeks [9]. This figure was then inflated by 40%, as was done for urinary losses, although the basis for this was not clear. The FNB/IOM committee applied a different conceptual approach to estimate intestinal losses of endogenous zinc. Ten data points were identified that measured total absorbed zinc and intestinal excretion of endogenous zinc using radioisotope or stable isotope techniques, where the absorbed zinc was estimated from a whole day's dietary intake [6,10–15]. Only data from North American or European men aged 19 to 50 years were accepted. These data demonstrated that the excretion of endogenous zinc via the intestine is strongly correlated with absorbed zinc. Therefore, to estimate the physiological requirement for absorbed zinc, it is necessary to consider the amount of intestinal losses of endogenous zinc that would occur when the absorbed zinc is just sufficient to offset the sum of all endogenous zinc lost from both intestinal and nonintestinal sites. The derivation of this requirement is illustrated in **figure 2** (excerpted from FNB/IOM [1]). Using this approach, the FNB/IOM committee estimated that 2.57 mg/day of endogenous zinc would be lost via the intestine and the total physiological requirement for absorbed zinc in adult men is 3.84 mg/day, after adding nonintestinal zinc losses.

IZiNCG concluded that the conceptual approach used by the FNB/IOM committee was the most appropriate. However, for the development of internationally applicable estimates of zinc requirements, it was justifiable to also include similar data from apparently healthy men and women, regardless of their age and nationality. Nine additional data points were identified [14,16–20], and the relationship between total absorbed zinc and intestinal losses of endogenous zinc for all 19 data points was examined by linear regression, weighting by sample size. The slope of the line derived from the 19 data points was not different from that derived from the original 10 data points used by FNB/IOM [4]; there was also no difference in the slopes of lines derived from data for studies of men vs. women. IZiNCG concluded that the most reliable estimate of the relationship between total absorbed zinc and intestinal losses of endogenous zinc should be based on the data from all 19 studies.

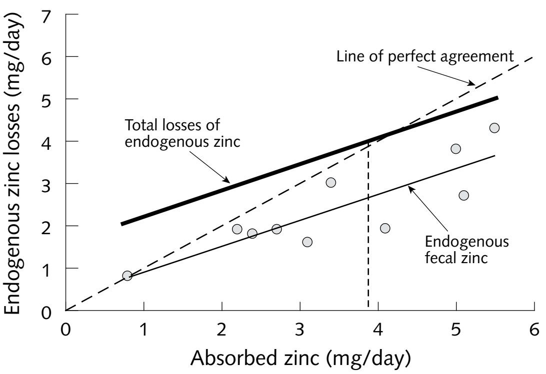

FIG. 2. Graphical representation of the conceptual model used by FNB/IOM [1] to estimate intestinal endogenous losses of zinc and total endogenous losses of zinc when the amount of absorbed zinc is sufficient to offset all losses. The 10 data points represent mean data from seven published studies of zinc absorption and intestinal losses of endogenous zinc in adult American or Western European men (19 to 50 years of age). The regression line (—) of the data points represents the relationship between total absorbed zinc and intestinal losses of endogenous zinc. The parallel line above (**—**) represents the total endogenous losses of zinc after adding the static losses through urine, integument, and semen. The line of perfect agreement (– – –) indicates where total endogenous losses would be equal to the amount of absorbed zinc. The vertical line (----) is derived from the point where the line for the total losses of endogenous zinc crosses the line of perfect agreement, thus representing the physiological requirement for absorbed zinc for North American adult men (3.84 mg/day)

One final consideration for the derivation of internationally applicable requirement estimates is that of reference body weights. The FNB/IOM committee used reference body weights for North American populations, whereas the WHO committees and IZiNCG used those based on the NCHS/CDC 1977 growth reference data that are more suitable for international use. IZiNCG felt it was unnecessary to correct intestinal losses or urinary losses for different body weights among adults. However, surface losses would be more directly associated with body size, so these were adjusted for body weight. Estimates for the various sources of endogenous losses of zinc for 65-kg adult men derived by IZiNCG are summarized in **table 1** and are compared with those derived by the WHO and FNB/IOM committees.

As shown graphically (**fig. 3**), IZiNCG estimated that 1.54 mg/day of endogenous zinc would be excreted via the intestine when the amount of absorbed zinc is equivalent to the total losses of endogenous zinc from all sources. Considering endogenous losses of zinc from nonintestinal sources (urine, 0.63 mg/day; surface, 0.42 mg/day; semen, 0.10 mg/day), the total physiological requirement for absorbed zinc in adult men was estimated to be 2.69 mg/day.

TABLE 1. Estimated physiological requirements for absorbed zinc in adult men and women as developed by expert committees of the World Health Organization (WHO), the US Food and Nutrition Board/Institute of Medicine (FNB/IOM), and the International Zinc Nutrition Consultative Group (IZiNCG)

Reference body weights, endogenous zinc losses, and additional requirements	WHO [2, 3]	FNB/IOM [1]	IZiNCG [4]
Men			
Reference body weight (kg)	65	75	65
Urinary excretion (mg/day)	0.30	0.63	0.63
Integument (mg/day)	0.30	0.54	0.42
Semen (mg/day)	—	0.10	0.10
Total nonintestinal endogenous losses (mg/day)	0.60	1.27	1.15
Intestinal excretion of endogenous zinc (mg/day)	0.80	2.57	1.54
Total endogenous losses (mg/day)	1.40	3.84	2.69
Women			
Reference body weight (kg)	55	65	55
Urinary excretion (mg/day)	0.30	0.44	0.44
Integument (mg/day)	0.20	0.46	0.36
Menstrual blood (mg/day)	—	0.10	0
Total nonintestinal endogenous losses (mg/day)	0.50	1.00	0.80
Intestinal excretion of endogenous zinc (mg/day)	0.50	2.30	1.06
Total endogenous losses (mg/day)	1.00	3.30	1.86
Additional requirements for pregnancy (1st, 2nd, 3rd trimesters) (mg/day)	0.1, 0.3, 0.7	0.16, 0.39, 0.63	0.70[a]
Additional requirements for lactation (0–3, 3–6, > 6 mo)(mg/day)	1.4, 0.8, 0.5	1.35[b]	1.0[b]

a. A single estimate for additional zinc requirements is applied throughout pregnancy.
b. A single estimate for additional zinc requirements is applied throughout lactation.

Adult women

Some specific figures for endogenous zinc losses differ by sex, as summarized below. For urinary losses, the WHO committees used data from one study of women with very restricted zinc intakes and then increased that figure by 40%, as was done for men. The FNB/IOM committee used data from 10 published studies estimating the mean urinary zinc excretion at 0.44 mg/day for adult women. IZiNCG accepted the figure used by the FNB/IOM. Each of the expert committees estimated women's surface losses of zinc using data for adult men and adjusting for differences in reference body weight. For adult women, IZiNCG estimated these losses at 0.0065 mg zinc/kg body weight/day × 55 kg = 0.36 mg zinc/day.

There is little information on endogenous zinc losses in menstrual fluid. In one study [21], the average excretion of menstrual fluid in one cycle was 60 g, with a mean zinc content of 2.8 μg/g fluid, resulting in a loss of 0.005 mg zinc/day. The WHO committees did not account for menstrual zinc losses. The FNB/IOM committee reported average menstrual losses to be 0.1 mg/day, but this was based on erroneous interpretation of data from the aforementioned study [21]. Because loss of zinc by this route is negligible, IZiNCG concluded that it need not be considered in estimates of zinc requirements.

As discussed above, IZiNCG preferred the conceptual approach used by the FNB/IOM committee to esti-

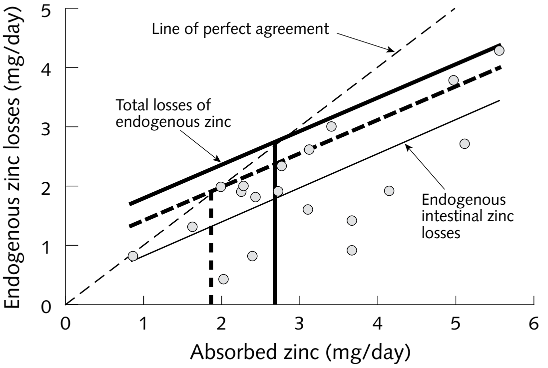

FIG. 3. Graphical representation of the model used by IZiNCG [4] to estimate intestinal and total endogenous losses of zinc when the amount of absorbed zinc is sufficient to offset all losses. The 19 data points represent mean data from 12 published studies in adult men and women 19 to 50 years of age. The regression line (—) of the data points represents the relationship between total absorbed zinc and intestinal losses of endogenous zinc. The parallel lines above (— men, - - - women) represent the total endogenous losses of zinc after adding the static losses through urine, integument, and semen. The line of perfect agreement (- - -) indicates where total endogenous losses would be equal to the amount of absorbed zinc. The vertical lines (— men, - - - women) are derived from the point where the line for the total losses of endogenous zinc crosses the line of perfect agreement, thus representing the physiological requirement for absorbed zinc for a 65-kg adult man (2.69 mg/day) and a 55-kg adult woman (1.86 mg/day)

mate fecal losses of endogenous zinc. The endogenous losses of zinc by intestinal and nonintestinal routes for a 55-kg adult woman are summarized in **table 1**, and the IZiNCG estimated daily physiological requirement for adult women was 1.86 mg/day (**fig. 3**).

Additional requirements during pregnancy. To account for additional zinc requirements during pregnancy for synthesis of fetal and maternal tissue, the FNB/IOM and WHO committees derived estimates from one study [22]. FNB/IOM estimated these additional zinc needs during each trimester as 0.16, 0.39, and 0.63 mg/day, respectively and WHO provided similar estimates (0.1, 0.3, and 0.7 mg/day, respectively). To provide a single figure for the additional absorbed zinc requirement throughout pregnancy, IZiNCG proposed using 0.7 mg/day, though recognizing that this single figure overestimates the average zinc requirement during the first and second trimesters.

Additional requirements during lactation. The transfer of zinc from mother to infant in breastmilk must be added to the physiological requirement for lactating women. This amount is determined from the average volume of breastmilk consumed by infants and the zinc concentration of breastmilk at different postpartum periods. The FNB/IOM committee used data for milk volumes determined among US women during the first year postpartum (0.78 L/day) and data from 12 studies of breastmilk zinc concentration at different postpartum time points (2.75 mg/L at 4 weeks, 2.0 mg/L at 8 weeks, 1.5 mg/L at 12 weeks, and 1.2 mg/L at 24 weeks). The FNB/IOM committee produced a single estimate of 1.35 mg/day additional absorbed zinc during lactation, after subtracting an assumed 1 mg/day of endogenous zinc that may become available during the first month postpartum because of involution of reproductive tissue. The WHO committees used data from just three studies to estimate the zinc content of human milk (2.5 mg/L at 1 month, 0.9 mg/L at 3 months, and 0.7 mg/L at 4 months) and estimated that an additional 1.4 mg zinc/day is needed from 0 to 3 months postpartum, 0.8 mg/day from 3 to 6 months, and 0.5 mg/day thereafter.

IZiNCG noted that the duration of breastfeeding patterns differs between the United States and developing countries and therefore used data derived from women in developing countries [23]. Because the zinc concentration of breastmilk is affected minimally by maternal zinc status, IZiNCG used the same data for breastmilk zinc content as the FNB/IOM. The amount of zinc excreted in breastmilk for different postpartum periods averages about 1 mg/day (**table 2**). Although more than this amount might be needed during the initial months, it may be partially offset by zinc released during involution of reproductive tissue, and IZiNCG estimated the additional requirement at 1 mg/day throughout lactation.

TABLE 2. Amount of zinc transferred from mother to child in human milk according to child's age

Age (mo)	Milk volume (mL/day)[a]	Zinc concentration (mg/100 mL)[b]	Zinc amount (mg/day)
0–2	714	0.230	1.64
3–5	784	0.135	1.06
6–8	776	0.120	0.93
9–11	616	0.120	0.74
12–23	549	0.120	0.66

a. Data from Brown et al. [23].
b. Data from FNB/IOM [1].

Children

Infants 0 to 6 months. Little information is available on the physiological requirements for absorbed zinc in infants less than 6 months of age. The FNB/IOM committee did not estimate physiological zinc requirements for this group but instead described adequate intakes (AIs) based on the average amount of zinc derived from breastmilk. Using average figures for zinc transfer in breastmilk from 0 to 5 months postpartum, the FNB/IOM proposed 2.0 mg/day as the AI for infants under 6 months of age. The WHO committees developed estimates for young infants by extrapolating from data for adults and adding the amount of zinc needed for growth, and estimated the absorbed zinc requirement for infants 0 to 5 months of age to be from 0.7 to 1.3 mg/day, depending on age and sex. Considering available information, IZiNCG concluded that breastmilk is a sufficient source of zinc for exclusively breastfed, normal birthweight, term infants until about 6 months of age. Non-exclusively breastfed infants need to absorb approximately 1.3 mg/day during the first 3 months of life and 0.7 mg/day from months 3 to 5.

Less information is available on the zinc requirements of infants with low birthweight, but they probably have greater needs for absorbed zinc than normal birthweight infants because of higher rates of postnatal growth and more limited hepatic zinc reserves at birth, which may normally be used to partially meet postnatal requirements [24]. Also, growth rates in low-birthweight infants increased when they were provided with 2 to 5 mg of supplemental zinc/day [25–27]. More research is needed to estimate zinc requirements in this group.

Children 6 months to 18 years. The FNB/IOM used a factorial method to estimate physiological zinc requirements of older infants and children. Losses of endogenous zinc from nonintestinal sites (i.e., urinary and surface losses) extrapolated from adults were estimated to be 0.014 mg/kg/day. Intestinal losses of endogenous zinc were estimated to be 0.050 mg/kg/day for infants 6 to 11 months of age, based on a study of breastfed infants, and 0.034 mg/kg/day for older children, as extrapolated from adult data. Additionally, the amount of zinc required for growth was determined based on 0.020 mg zinc/g of tissue accrued. These figures were extrapolated for each age group based on reference body weights. For male adolescents 14 to 18 years of age, zinc losses in semen (0.1 mg/day) were also added to the requirement, as for adult men. The WHO committees estimated physiological zinc requirements throughout childhood by extrapolating from the data used to estimate endogenous losses in adults.

IZiNCG also used the factorial approach, but based intestinal losses of endogenous zinc on their own estimates and used the NCHS/CDC/WHO reference body weights (**table 3**). The extrapolated estimates were based on the following: urinary losses, 0.0075 mg/kg/day; surface losses, 0.0065 mg/kg/day; intestinal losses, 0.05 mg/kg/day for infants 6 to 12 months or 0.02 mg/kg/day for children 1 year of age and older.

Daily zinc intake requirements and recommended intake levels

To translate physiological requirements for absorbed zinc into recommendations for daily dietary zinc intakes, it is necessary to take into account the proportion of zinc in the diet that is absorbed by the intestine (**fig. 1**). The following sections present a review of the dietary factors that affect zinc absorption, estimates of zinc absorption from different diets, and the resultant derivation of dietary zinc intake requirements.

Dietary sources of zinc and estimates of zinc absorption

Zinc occurs in a wide variety of food sources but is found in highest concentrations in animal-source foods (0.5 to 6.1 mg/100 g), particularly in organs, meat, fish, and shellfish, with lesser amounts in eggs and milk (0.4 to 3.1 mg/100 g). Zinc content is relatively high in nuts, seeds, legumes, and whole-grain cereals (0.5 to 7.8 mg/100 g) and is lower in tubers, refined cereals, fruits, and vegetables (0 to 0.9 mg/100 g).

To quantify the proportion of zinc that is available for absorption from typical diets, one has to consider the impact of dietary factors that modulate zinc absorption and the dietary sources of those factors. Dietary components that inhibit zinc absorption are phytate and calcium, whereas protein enhances zinc absorption [28, 29]. Also, increasing the amount of zinc in the diet results in a lower percentage of zinc absorbed [30], although the absolute amount of zinc absorbed increases.

Phytate is a mineral chelator occurring in plants, with a high content in cereal grains, nuts, and legumes and a lower content in other plant foods. Phytate is not digested or absorbed in the human intestine, so minerals, including zinc, that are bound to phytate may pass through the intestine unabsorbed. The phytate:zinc molar ratio of the diet is useful to estimate the proportion of absorbable dietary zinc. Seeds, nuts, legumes, and unrefined cereal grains have the highest phytate:zinc molar ratios (22 to 88), whereas other plant foods

TABLE 3. Estimated physiological requirements for absorbed zinc during childhood by age group and sex, as developed by expert committees of the World Health Organization (WHO), the US Food and Nutrition Board/Institute of Medicine (FNB/IOM), and the International Zinc Nutrition Consultative Group (IZiNCG)

WHO [2, 3]			FNB/IOM [1]			IZiNCG [4]		
Age, sex	Reference weight (kg)	Physiological requirement (mg/day)	Age, sex	Reference weight (kg)	Physiological requirement (mg/day)	Age, sex	Reference weight (kg)	Physiological requirement (mg/day)
6–12 mo	9	0.84	7–12 mo	9	0.84	6–11 mo	9	0.84
1–3 yr	12	0.83	1–3 yr	13	0.74	1–3 yr	12	0.53
3–6 yr	17	0.97	4–8 yr	22	1.20	4–8 yr	21	0.83
6–10 yr	25	1.12						
10–12 yr, M	35	1.40	9–13 yr	40	2.12	9–13 yr	38	1.53
10–12 yr, F	37	1.26						
12–15 yr, M	48	1.82						
12–15 yr, F	48	1.55						
15–18 yr, M	64	1.97	14–18 yr, M	64	3.37	14–18 yr, M	64	2.52
15–18 yr, F	55	1.54	14–18 yr, F	57	3.02	14–18 yr, F	56	1.98
Pregnancy	—	2.27	Pregnancy (1st, 2nd, 3rd trimester)	—	4.12, 4.42, 5.02	Pregnancy	—	2.68
Lactation	—	2.89	Lactation (0–3, 3–6, 6–12 mo)	—	4.92, 3.82, 4.52	Lactation	—	2.98

have lower phytate:zinc molar ratios (0 to 42).

Estimates of zinc absorption in adults from typical diets. WHO [2, 3] and FNB/IOM [1] estimated the percent absorption of zinc from usual diets using a similar conceptual approach, although the types of studies used differed markedly. Each extracted data from studies of zinc absorption and plotted the mean amount of absorbed zinc against the total zinc ingested from the meal or diet. A regression equation derived from these data was used to determine the amount of total dietary zinc needed to provide an amount equivalent to the physiological requirement. This amount of total dietary zinc represents the daily "estimated average requirement" from the diet, or the EAR. The percentage of zinc absorbed at this level of intake (physiological zinc requirement/total zinc intake × 100%) represents the "critical" average zinc absorption. IZiNCG [4] reviewed the methods used by the WHO and FNB/IOM committees to estimate zinc absorption, taking into consideration the methodology used to measure absorption, the types of diets and subjects from which data were derived, as well as the statistical models used.

Two general types of study designs have been used most commonly to estimate dietary zinc absorption: single-meal studies measuring absorption from a single test meal and total-diet studies measuring zinc absorption from multiple meals consumed over one or more days and to which subjects are usually equilibrated. Differences in the methodology have been described [4, 29], but essentially only total-diet studies allow for the estimation of true zinc absorption at the individual level, and studies using total-diet methodology should be considered the gold standard method for determining dietary zinc absorption. Indeed, a prediction equation for zinc absorption derived from single-meal studies systematically underestimated percent zinc absorption when compared with a prediction equation derived from studies of total diets [29].

In determining their zinc absorption estimates, the WHO committee used data from a combination of single-meal studies and total-diet studies, presumably mostly single-meal studies [2]. Available data were divided into three categories according to the phytate:zinc molar ratio of the test meal or diet (**table 4**). The FNB/IOM committee selected 10 data points from seven published total-diet studies of zinc absorption [1] from North American or Western European adult men only and from both mixed and semipurified formula diets. All data points were considered in a single diet category (**table 4**). The same regression line relating zinc intake and total absorbed zinc derived from the studies of men was later applied for women.

In their estimates, IZiNCG considered only data from total-diet studies, without geographic restriction, and included studies from adult women. IZiNCG rejected absorption studies that included semipurified diets or used exogenous zinc salts, as these do not represent typical diets consumed by populations, and the zinc absorption is expected to be higher from liquid formulas than from solid food matrices [31], and possibly higher from soluble zinc salts added exogenously than from an equivalent amount of zinc endogenous to the food. Seventeen data points from 11 published articles meeting the above criteria were identified. Zinc and phytate contents of the study diets were available or estimated for 15 studies, and calcium and protein contents were available for 12. The 15 data points for which at least zinc and phytate contents were available were

TABLE 4. Estimates of dietary zinc absorption, as developed by the World Health Organization (WHO), the US Food and Nutrition Board/Institute of Medicine (FNB/IOM), and the International Zinc Nutrition Consultative Group (IZiNCG) and summaries of the data used to derive them

Variable	WHO [2, 3]			FNB/IOM [1]	IZiNCG [4]	
Diet types represented	Highly refined[a]	Mixed/ refined vegetarian[b]	Unrefined[c]	Mixed ($N = 5$) Semipurified ($N = 4$) EDTA-washed soy protein ($N = 1$)	Mixed ($N = 11$) Refined vegetarian ($N = 3$)	Unrefined, cereal-based ($N = 1$)
Study type	Single meal and total diet			Total diet		
Subjects	NA	NA	NA	Men 19–50 yr	Men and women 20+ yr	Men and women 20+ yr
Phytate:zinc molar ratio	< 5	5–15	> 15	NA	4–18	> 18
Zinc absorption[d]	50%	30%	15%	41%	26% men, 34% women	18% men, 25% women

EDTA, ethylenediaminetetraacetic acid; NA, not available

a. Refined diets low in cereal fiber, and where animal foods provide the principal source of protein. Includes semipurified formula diets.

b. Mixed diets and lacto-ovo-vegetarian diets that are not based on unrefined cereal grains or high-extraction-rate (> 90%) flours.

c. Cereal-based diets, with > 50% of energy intake from unrefined cereal grains or legumes and negligible intake of animal protein.

d. These figures represent the "critical" level of zinc absorption, or that which occurs when zinc intakes are just sufficient to meet physiological requirements for absorbed zinc.

used in the final analyses [14–20, 32, 33] (**table 4**).

This analysis [4] used a logit regression model and determined that neither protein nor calcium added significant predictive power, so the final model ($r^2 = 0.413$, $p < .001$) included only zinc and the phytate:zinc molar ratio, both of which were highly significant predictors of percent zinc absorption. Therefore, it appears to be valid to continue to use the phytate:zinc molar ratio to predict zinc absorption from diets. The prediction equation for the fraction of absorbable zinc derived from this model is

$$\text{Logit FAZ} = 1.1365 - 0.6129 \times \ln(\text{mg zinc}) - 0.3164 \times \ln(\text{phytate:zinc molar ratio})$$

and

$$\text{Fraction of absorbed zinc} = \frac{\exp(\text{logit FAZ})}{1 + \exp(\text{logit FAZ})}$$

where logit FAZ is the logit of fractional zinc absorption, ln is the natural log, and exp is the exponential.

IZiNCG divided diets into two categories based on the phytate:zinc molar ratios, using 18 as a cut-point (**table 4**). For each diet category, the phytate:zinc molar ratio at the midpoint of the range (i.e., 11 for mixed diets and 24 for cereal-based diets) and the percent absorption of zinc associated with a wide range of total zinc intakes was used to calculate the amounts of absorbed zinc, using the equation above; the relationship between total zinc intake and absorbed zinc for the two diet categories is shown in **figure 4**. Using the IZiNCG physiological requirement for absorbed zinc of adult men (2.69 mg zinc/day) and women (1.86 mg zinc/day), the total dietary zinc intake requirement was determined for each diet type (**fig. 4**). The critical levels of zinc absorption were 26% for men and 34% for women for mixed/refined vegetarian diets, and 18% for men and 25% for women for unrefined, cereal-based diets. The figures for zinc absorption that correspond to the amount of ingested zinc needed to meet the physiological requirements of adult men and women with higher reference body weights assumed by the FNB/IOM committee (i.e., 75 kg for men and 65 kg for women) are 24% (men) and 31% (women) for those consuming mixed/refined vegetarian diets and 16% (men) and 22% (women) for those consuming unrefined, cereal-based diets. These estimates of zinc absorption are considered tentative until further data are available from a wider range of diet types, particularly from unrefined diets with a high phytate:zinc molar ratio (i.e., > 18), for which only one data point was identified.

Since the IZiNCG algorithm was published, six new data points from three studies of zinc absorption in adults meeting the IZiNCG criteria above have been identified [34–36]. Three of the diets studied had a phytate:zinc molar ratio greater than 18 and three of 18 or less. For those data points with phytate:zinc molar ratio greater than 18, the IZiNCG algorithm somewhat overestimated the percent zinc absorption (20%, 21%, 27%) as compared with the observed levels (15% and 14% in men [34] and 22% in women [35], respectively). Nonetheless, the observed values were close to the mean absorption value of 18% for men and 25% for women used by IZiNCG for the unrefined, cereal-based diet category. For those with phytate:zinc molar ratio of 18 or less, the algorithm somewhat underestimated absorption (26%, 26%, and 35%) as compared with observed levels (29% and 38% in men [34] and 38% in women [36], respectively). Nonetheless, these were close to the mean absorption value of 26% for men and 34% for women consuming mixed/refined vegetarian diets. **Figure 5** shows the relationship between total zinc intake and observed, absorbed zinc (adjusted for total zinc and phytate:zinc molar ratio of the diet) for those data points used to

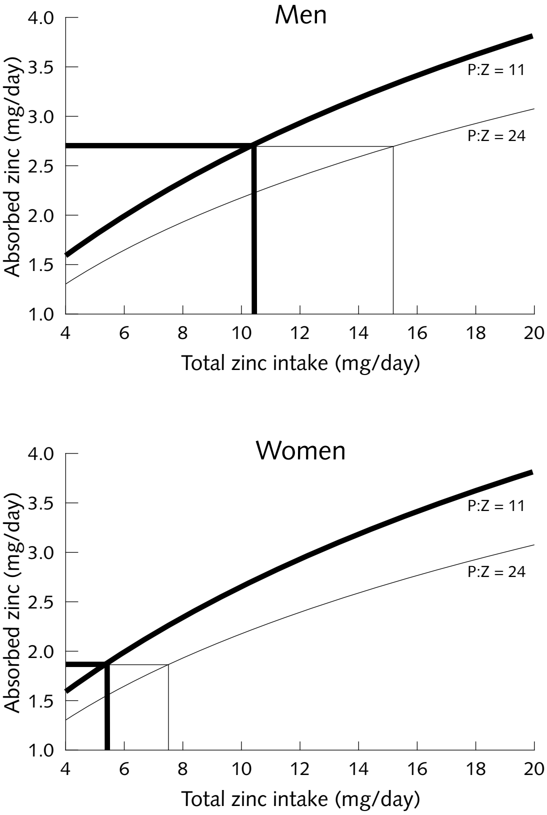

FIG. 4. Derivation of the estimated average requirement for men (upper panel) and women (lower panel) and critical level of zinc absorption for mixed/refined vegetarian diets and unrefined cereal-based diets, using the association between total zinc intake and absorbed zinc for each diet type and the physiological requirement. P:Z, phytate:zinc molar ratio

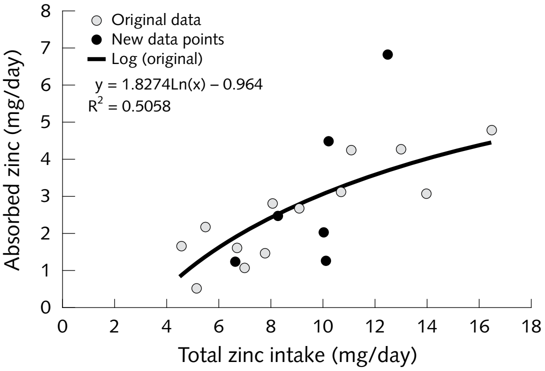

FIG. 5. Association between total zinc intake (mg/day) and absorbed zinc (mg/day) adjusted for phytate:zinc molar ratio in adults for original data points used to derive the IZiNCG algorithm for predicting absorbed zinc, and new data points appearing since the algorithm was published

derive the IZiNCG algorithm, overlaid with the new data points described above. Although the new data fit generally well, the IZiNCG predictive equation should be updated as more data accumulate for zinc absorption from different diet types.

Zinc absorption during pregnancy. The WHO committees did not propose different levels of zinc absorption for pregnant or lactating women. The FNB/IOM committee concluded that zinc absorption is not increased significantly during pregnancy. This was based on the results of one study in which zinc absorption was measured prior to conception and at 24 to 26 weeks and 34 to 36 weeks of gestation [37], with average zinc intakes of 15 mg/day throughout the study. The increase from 15% absorption at preconception to 19% during pregnancy was not statistically significant. Although it is still possible that zinc absorption in pregnancy increases when zinc intakes are lower, IZiNCG concurred with the FNB/IOM committee that there is presently insufficient evidence to suggest a different level of zinc absorption for pregnant women from that for nonpregnant women.

Zinc absorption during lactation. The efficiency of zinc absorption does appear to increase significantly during lactation [37–40]. In one study [37], zinc absorption was 10 percentage points greater among healthy, North American, lactating women ingesting 15 mg zinc/day than among women in a nonpregnant, nonlactating, control group. The FNB/IOM committee suggested a level of absorption for lactating women that was 10% greater than that for nonlactating women on the basis of that study. IZiNCG considered two other studies [38, 40] that reported higher zinc absorption values among lactating women 15 and 19 percentage points above their nonlactating counterparts, both with intakes of about 8 mg zinc/day. As there is insufficient information to determine whether these latter lactating women were meeting their dietary zinc requirements, IZiNCG preferred the more conservative estimate of 10% increased absorption [37]. Therefore, IZiNCG estimates for lactation were 44% (≥ 19 years of age) and 40% (14 to 18 years of age) for those consuming mixed/refined vegetarian diets and 35% (≥ 19 years of age) and 32% (14 to 18 years of age) for those consuming unrefined, cereal-based diets.

Zinc absorption in children. As the percentage of dietary zinc absorbed is partly determined by the amount of zinc in the diet, and children's intake requirements are proportionately lower than those of adults, equations used to predict zinc absorption in adults cannot be applied directly to predict zinc absorption in children. Unfortunately, there are still limited data available on the percent zinc absorption from diets among children of different ages. The FNB/IOM committee applied lower figures for the critical absorption level for children than they used for adults based on data from only two studies of single meals [41, 42] where the mean zinc absorption was 30%. IZiNCG felt there was no present justification for assuming different levels of zinc absorption for different age groups, and therefore, for each diet type, the mean of the absorption estimates for adult men and women was applied to children 1 to 18 years of age (i.e., 31% absorption from mixed/refined vegetarian diets and 23% from unrefined, cereal-based diets).

Since the time of the IZiNCG report, two other published studies of zinc absorption from diets among preadolescent children (9 to 12 years of age) providing three data points were identified [43, 44]. The diet for one data point had a phytate:zinc molar ratio greater than 18, and the diet for the other two had a phytate:zinc molar ratio of 18 or less. A single log equation derived from these points, regardless of phytate:zinc molar ratio, yielded an r^2 of 0.895 and was lower than but parallel to a similarly derived curve with the data points used by IZiNCG to estimate zinc absorption in adults (**fig. 6**). As for adults, the proportion of zinc absorbed decreases as zinc intake increases. Based on this log equation for preadolescent children, the predicted zinc absorption level at an intake close to the EAR for this age group (i.e., 5 to 7 mg/day) was about 30%, in the range suggested by FNB/IOM and IZiNCG.

Four new data points of zinc absorption from diets among preschool children (4 years of age) were also identified [45, 46]. Two of the diets had phytate:zinc molar ratios greater than 18, and two diets had phytate:zinc molar ratios of 18 or less. Again, fractional zinc absorption decreased with increasing zinc intakes [46]. A log equation derived from these four points (r^2 = 1.00) predicted 33% absorption at a zinc intake level of 3.5 mg/day, representing the average EAR for children of this age for the two diet types (i.e., 3 to 4 mg/day) (**fig. 6**).

Further studies of zinc absorption in children from

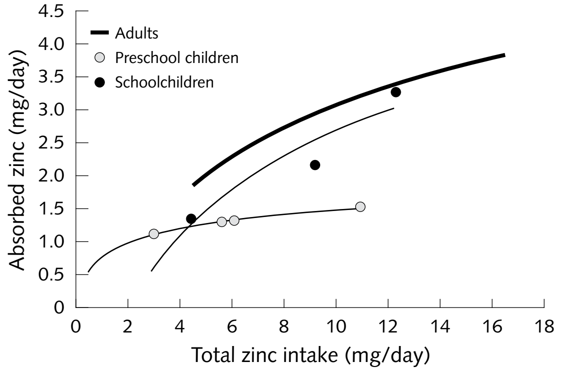

FIG. 6. Association between total zinc intake and observed amount of absorbed zinc in studies of zinc absorption from total diets among preschool and school-aged children and adults

a variety of typical diets are needed to improve these estimates and to quantify the effect of the phytate: zinc molar ratio on absorption efficiency. Nonetheless, available data suggest that the absorption figures for children presented by IZiNCG are reasonable. Although the estimate of 23% absorption for unrefined cereal-based diets is not substantiated by these curves, it may be prudent to assume 23% absorption for this diet type until further data are available.

Derivation of the estimated average requirements for zinc

The estimates for absorption can now be applied to the physiological requirements for absorbed zinc to derive EARs and, subsequently, the recommended daily allowances (RDA) for dietary intakes of zinc. Methods for calculating these reference intake values and their uses have been described previously by the FNB/IOM Dietary Reference Intake Committees [47]. Only the EARs for zinc, as presented by IZiNCG for international use, are presented below, as the EAR is relevant for population zinc assessment. The RDAs for zinc, as determined by IZiNCG, are used only for the dietary intake assessment of individuals and were described previously [4].

The EAR represents the mean dietary requirement, or the dietary intake level at which 50% of individuals would meet their physiological requirement. The EAR is derived by dividing the mean physiological requirement for absorbed zinc by the estimated average absorption of zinc (**fig. 1**). For example, the EAR for adult women (55 kg) consuming unrefined, cereal-based diets would be calculated as 1.86 mg absorbed zinc/day ÷ 0.25 = 7.4 mg zinc/day, and rounded to 7 mg/day. The EAR for all age, sex, and life-stage groups is given in **table 5** for both mixed/refined vegetarian diets and unrefined, cereal-based diets.

TABLE 5. IZiNCG [4] Estimated average requirement (EAR) for dietary zinc intake according to life stage and diet type

			IZiNCG EAR for zinc (mg/day)	
Life stage	Sex	Reference body weight (kg)	Mixed or refined vegetarian diets	Unrefined, cereal-based diets
6–11 mo	M + F	9	3	4
1–3 yr	M + F	12	2	2
4–8 yr	M + F	21	3	4
9–13 yr	M + F	38	5	7
14–18 yr	M	64	8	11
14–18 yr	F	56	7	9
Pregnancy	F	—	9	12
Lactation	F	—	8	9
> 19 yr	M	65	10	15
> 19 yr	F	55	6	7
Pregnancy	F	—	8	10
Lactation	F	—	7	8

For breastfeeding infants 7 to 11 months of age, the FNB/IOM committee assumed that 50% of zinc in breastmilk is absorbed [48] and that the average breastmilk intake is 0.76 L/day. The amount of zinc required from complementary foods was then determined by difference, assuming 30% zinc absorption from foods. The EAR for breastfed children was calculated as the amount of zinc acquired from breastmilk plus that required from complementary foods. The WHO committees assumed that the absorption of zinc from breastmilk was 80%, although this was not based on direct measures of absorption, and estimates of zinc intake from breastmilk in exclusively breastfed infants were derived from one study of infants 1 to 3 months of age [49]. The IZiNCG committee used a similar approach as the FNB/IOM, also assuming 50% absorption of zinc from breastmilk. However, different estimates for average breastmilk consumption and milk zinc concentrations were used (**table 2**). The calculated total zinc requirements were somewhat lower than those derived when it is assumed that all dietary zinc is from complementary foods. IZiNCG felt that it was unnecessary to provide two different sets of EARs for breastfed and nonbreastfed children, and therefore the slightly higher EARs derived for complementary fed children were recommended for all children of this age group (**table 5**).

Determining the prevalence of inadequate zinc intakes in populations

Measurement of zinc intakes

Standard dietary assessment methods can be used to estimate dietary zinc intakes in a population. Weighed food records and 24-hour dietary recalls are recommended methods. An interactive 24-hour recall method has been specially designed for measuring usual intakes of total and absorbable zinc in lower-income countries [50]. Semiquantitative food-frequency questionnaires have not yet been validated for the estimation of usual zinc intakes by individuals.

Assessing the adequacy of zinc intakes

To evaluate the adequacy of dietary zinc in populations, intakes must be compared with an appropriate set of dietary reference values, taking into account the estimated bioavailability of dietary zinc. The EARs can be used to evaluate the risk of inadequate intakes by a population by determining the proportion of the population whose intakes fall below the EAR. The application of the EAR in assessment of adequacy of zinc intakes by populations will be discussed in further detail below.

To correctly determine the prevalence of persons with intakes below the dietary requirement level, it is necessary to work with a distribution of *usual* intakes. This requires that at least two nonconsecutive days of dietary intake data are collected for each individual in the sample, or for at least a subset of individuals. The usual intake of a population requires that the difference in nutrient intake by individuals that occurs from day to day is estimated and removed, leaving an adjusted distribution representing the variation in intakes between individuals. If the intake distribution is not adjusted, it will be inappropriately wide, and the percentage of the population with intakes below a fixed, lower cutoff will be overestimated. Statistical methods to make this adjustment have been described [47, 51–53]. Once the adjusted distribution is derived, either the *probability* or the *prevalence* of intakes below the EAR can be determined.

The probability approach and its underlying assumptions have been described previously [47, 51]. To use this method, it is necessary that the distribution of the requirements is known and is symmetrical about the mean, and that the physiological requirements for the nutrient are independent of its intake. The coefficient of variation of zinc requirements has been estimated to be 12.5% [2, 4]. Independence of zinc requirements and intakes can be assumed [4].

The prevalence of intakes below the EAR can also be estimated by using the EAR cut-point method. Theoretical aspects and application of this methodology have been described [47, 54]. Briefly, the requirements for use of this method are the same as those indicated for the probability approach but include an additional requirement that the variability in intakes among individuals in a population is greater than the variability in requirements of individuals. The latter is assumed to be valid for zinc in most cases, as the coefficient of variation of the distribution of population zinc intakes (**table 6**) usually exceeds the assumed coefficient of variation of 12.5% of the zinc requirement distribution. The accuracy of this method can approach that of the probability method, particularly when the actual prevalence of the inadequate intakes is neither very high nor very low.

In the case that only 1 day of intake was determined

TABLE 6. Examples from studies of dietary zinc intakes with intraindividual variation removed and the associated coefficient of variation of the adjusted distribution of usual zinc intakes

Country	Sex	Age range (yr)	*N*	Mean + SD zinc intake (mg/day)	Coefficient of variation of adjusted distribution (%)[a]
United Kingdom [2, 56]					25
United States [55]	M + F	0–< 1	898	6.6 + 2.3	34.8
		1–3	3,908	7.6 + 3.3	43.4
		4–5	2,668	9.1 + 3.7	40.7
Egypt [57]	M + F	1.5–2.5	96	5.2 + 1.6	30.4[b]
Kenya [57]	M + F	1.5–2.5	100	3.7 + 0.9	23.7[b]
Ghana [58]	M + F	3–6	148	4.7 + 1.1	23.4
Malawi [58]	M + F	4–6	67	6.6 + 1.7	25.8
Mexico [57]	M + F	1.5–2.5	59	5.4 + 1.3	25.0[b]
Papua New Guinea [59]	M + F	6–10	67	4.4 + 1.3	29.5
Malawi [59]	F (pregnant)	14–45	60	6.8 [SD not available]	23

a. The usual zinc intake distribution was adjusted by removing variance due to intraindividual intake variability, unless otherwise indicated.

b. The intake distribution was determined by using the mean of at least 6 days of dietary intake data for each individual, rather than using a statistical adjustment for variation in intraindividual intake.

for each individual in the sample, it would be necessary to make assumptions about the width of the distribution of usual intakes for that population. The coefficient of variation of adjusted distributions of usual intakes derived from other similar populations may be applied. Several data sets for which a corrected intake distribution has been determined indicate that the coefficient of variation of the distribution is often about 25% (**table 6**). The coefficient of variation was notably higher among children in the United States [55], but this may be attributed to the availability of zinc-fortified foods in the population.

Assuming then that the SD of the intake distribution is 25% of the mean, the proportion of individuals with intakes below the EAR can be determined using a cumulative distribution function, providing an estimate of the prevalence of inadequate intakes. Caution must be used in the interpretation of these data; if the true distribution had a coefficient of variation much less than or greater than 25%, the proportion of the population with intakes below the EAR would be overestimated or underestimated, accordingly. Nonetheless, it has been argued that applying assumptions about the width of the usual intake distribution is preferable to not applying any adjustment [60].

IZiNCG recommended that when the probability of inadequate intake is 25% or more, or where 25% or more of individuals in the population have intakes less than the EAR, it may be considered that there is an elevated risk of zinc deficiency in the population and therefore is of public health concern. Although this cutoff is largely arbitrary due to lack of experience in evaluating zinc status and adequacy of dietary zinc intakes in populations, it will serve as a starting point to rank the relative risk of populations and may be refined after more data from diverse populations become available.

Evidence for the validity of dietary zinc requirements

Although the recommendations presented above for physiological and dietary requirements are based on reliable scientific methods, they still contain a theoretical component, as they were derived from a limited number of controlled, clinical studies with a relatively small number of subjects. It is therefore of interest to consider information on zinc intakes from a broader base of studies and surveys, taking into account the likely zinc status of the group as determined by biochemical or functional indicators of zinc status or measures of zinc homeostasis. This evidence will serve as an external validation of the zinc intake recommendations and help to identify areas where the recommendations may need to be refined.

Evidence for the validity of the IZiNCG physiological requirements

Data from several controlled clinical studies were used by IZiNCG to define the physiological requirements for absorbed zinc, based on measurement of daily losses of endogenous zinc. In this section, the results from these same studies, as well as other controlled clinical studies, are examined to assess zinc status at different levels of absorbed zinc intake to determine at what level adequate zinc status is, or is not, achieved. The studies used were mostly zinc depletion/repletion studies in which measures of zinc balance and/or some biochemical or functional indicators of zinc status were determined. A few other studies measured zinc absorption from different diet types and included at least one biochemical indicator of zinc status. Relevant information from these studies for men and women is summarized in Appendix 1.

Seventeen data points from studies in men and seven data points from studies in women were identified. To be included, subjects had to have received the diet for at least 1 week before zinc status measurements were made. In many of these studies, zinc absorption was measured directly from total diets by isotopic methods. Where zinc absorption was not measured, the total zinc intake reported for the study and a reported or estimated phytate:zinc molar ratio were used to estimate the absorbable zinc intake using the IZiNCG algorithm (see *Estimates of zinc absorption in adults from typical diets*). Highly refined zinc depletion diets were assigned a phytate:zinc molar ratio of 1. The zinc status of the subjects was then categorized according to the following criteria:

Zinc deficiency. All or most subjects having fasting serum zinc concentration below the lower limit (< 70.0 μg/dL as reported for women or, where possible, < 74.0 μg/dL for men as the IZiNCG suggested cutoff if raw data were available) and zinc balance not achieved in most or all subjects.

Marginal zinc status. Some subjects with fasting serum zinc concentration below the lower limits, as defined above, or evidence of zinc deficiency determined by other biochemical or functional indicators of zinc status, and mean zinc balance close to zero or zinc balance achieved in only some subjects.

Zinc adequacy. All or most subjects with serum zinc concentrations above the lower limit, as defined above, or other biochemical or functional indicators suggesting zinc adequacy, and all or most subjects achieving zinc balance.

As only half of the population is expected to truly meet their requirements at the mean physiological requirement level, absorbed zinc intakes in studies where *marginal* zinc status was achieved should be close to the true physiological requirement.

For studies in adult men, zinc deficiency was clearly present when the amount of absorbed zinc was less than 1.0 mg/day. Zinc status appeared to be marginal when absorbed zinc was between 1.0 and 2.63 mg/day. At levels above 2.0 mg/day, there was no evidence for reduced urinary losses of zinc. Reductions in urinary zinc losses have usually only been noted to occur at levels of zinc intake below the requirement level [1], and in this context may be used as an indicator of inadequacy. In the study by Turnlund et al. [12], although all male subjects maintained serum zinc concentrations within the normal range, the absorbed zinc amount of 2.63 mg/day did not allow subjects to achieve zinc balance after 2 weeks on the diet. On the other hand, in the study by Wada et al. [15], an intake of 2.8 mg/day of absorbable zinc maintained baseline urinary zinc excretion levels and serum zinc concentrations, and five of the six male subjects were able to maintain zinc balance. All studies with absorbed zinc of 2.8 mg/day or more demonstrated zinc adequacy. There appears to be a wide range of absorbed zinc levels where marginal zinc status was apparently achieved. These studies suggest that the requirement for adult men proposed by IZiNCG of 2.69 mg/day of absorbed zinc is a good estimate of true zinc requirements by men. This estimate appears to be on the conservative end of the range of marginal intakes. Data points for the amount of absorbed zinc categorized by zinc status are shown in relation to the physiological requirement for absorbed zinc for adult men (**fig. 7**).

Studies among adult women have not included absorbed zinc levels low enough to produce frank zinc deficiency (Appendix 1). In one study with estimated zinc absorption of 1.6 mg/day, although the mean plasma zinc concentration was maintained well above the lower limit, it was reported that zinc balance, as determined by mass balance, was marginal [61]. In another study with estimated zinc absorption of 1.8 mg/day, there was some evidence for marginal zinc status according to functional biochemical indicators, but not static biochemical indicators (i.e., plasma zinc concentration) [62, 63]. These data are more difficult to interpret, as some subjects simultaneously received a low-copper diet (1 mg/day). For example, extracellular copper-zinc superoxide dismutase activity decreased significantly when the zinc depletion diet was also low in copper, but not when copper intakes were adequate. The activity of this enzyme increased significantly after the zinc repletion diet was initiated. Both of these studies also have the limitation of not having measured zinc absorption directly. In another study in which women absorbed 2.3 mg zinc/day, there were no biochemical or functional signs of deficiency, and zinc balance was marginal [18]. The results from the two studies with estimated absorbed zinc intakes of 1.6 and 1.8 mg/day suggest that the physiological requirement proposed by IZiNCG of 1.86 mg/day may be a good, conservative estimate of the true mean requirement of adult women.

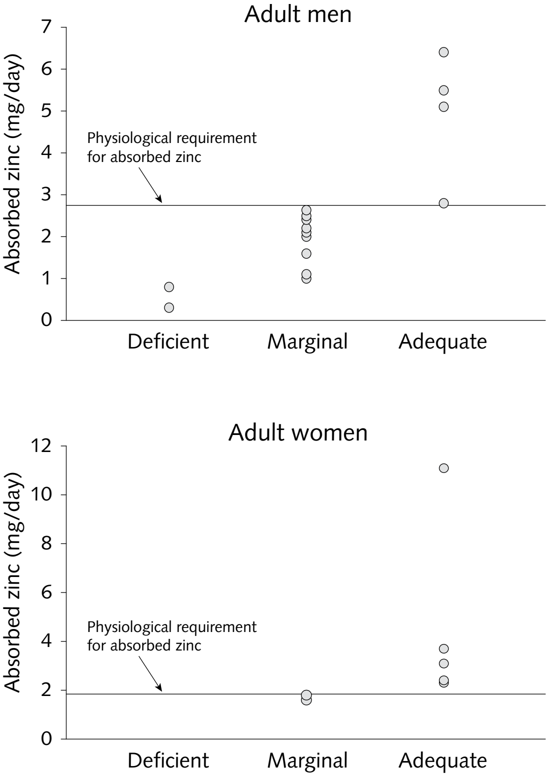

FIG. 7. Measured or estimated amount of absorbed zinc for groups of experimental subjects categorized by zinc status and shown in relation to the physiological requirement for absorbed zinc for adult men (upper panel) and women (lower panel). Details of the data sources are given in Appendix 1

The amount of absorbed zinc according to assigned zinc status is shown in **figure 7**.

For children, only a few studies have determined zinc homeostasis and zinc status at different levels of zinc intake. One study among girls 9 to 14 years of age compared zinc absorption, zinc balance, and serum zinc concentrations from a diet with either 4.4 or 12.3 mg zinc/day, both of which had a phytate:zinc molar ratio of 1 [44]. The amount of zinc absorbed was 1.3 mg/day on the low-zinc diet and 3.3 mg/day on the high-zinc diet. On the low-zinc diet, fasting plasma zinc concentration remained above the cutoff for this age group in all of the girls, and no decrease in urinary zinc excretion was observed. However, it was noted that zinc balance was significantly less than zero on the low-zinc diet, and significantly greater than zero on the high-zinc diet and leaving sufficient excess to cover theoretical requirements for growth. Although the latter result may indicate that 1.3 mg/day of absorbed zinc was marginal, it is possible that full adaptation to the lower zinc content was not achieved in the 2-week adaptation period. A group of healthy Malawian children 9 to 12 years of age absorbed a mean of 2.2 mg of zinc/day [43]. Zinc balance was positive for these children and left enough reserve to cover growth requirements, suggesting adequacy. Until further data are available for this age group, the theoretical estimate of the physiological requirement for absorbed zinc of 1.53 mg/day proposed by IZiNCG seems appropriate.

A study conducted among 3- to 4-year-old Peruvian children, selected based on their likelihood of zinc deficiency, measured zinc absorption in three groups of children who received a diet with one of two levels of zinc fortificant added to wheat flour or a non-zinc-fortified diet for about 50 days [46]. At the lowest zinc intake level of 2.98 mg/day (non-zinc-fortified), the measured amount of absorbed zinc was 1.1 mg/day, whereas at the higher intakes (5.59 and 10.95 mg zinc/day), the amount of absorbed zinc was higher (1.3 and 1.5 mg/day, respectively). After the feeding trial, approximately 10% of children on the lowest zinc intake level had low serum zinc concentrations (< 65 μg/dL), whereas none of the children on the higher-intake diets had low serum zinc; at baseline the prevalence of low serum zinc was approximately 20% in each of the groups. Although the 1.1 mg/day of absorbed zinc determined in this study may be considered adequate, there is insufficient evidence to accept or refute the theoretical physiological requirement estimate proposed by IZiNCG of 0.83 mg/day for 3- to 6-year-old children.

Although the study results described above provide some evidence of the appropriateness of the physiological zinc requirements presented by IZiNCG, further data from clinical studies among children are required to refine the theoretical estimates.

Evidence for the validity of the IZiNCG estimated average requirements for total zinc intake

The validity of the EARs relies on having reasonable estimates of both the physiological requirement for absorbed zinc and the fractional absorption of zinc. Cross-sectional studies reporting total dietary intake and providing some biochemical evidence of zinc status were reviewed for conformity between the two indicators in estimating the risk of zinc deficiency; relevant data are summarized in Appendix 2. Studies were chosen from those in which the dietary zinc intake represented the usual zinc intakes of the participants in their free-living habitats or, in a few cases, the subjects were habituated to the diet provided by the study.

For several reasons, evidence from these types of studies is difficult to interpret. In many cases, only the mean zinc intakes and mean serum zinc concentrations were given, but the proportion of individuals with serum zinc below an appropriate cutoff was not reported. Zinc intakes were sometimes expressed relative to an RDA, which does not give an estimate of prevalence of low intakes. For the purposes of review and comparison of these studies, the percentage of individuals with intakes below the appropriate EAR were estimated on the assumption that the coefficient of variation of the zinc intake distribution was 25%. In most cases, the bioavailability category was assumed, based on characteristics of the diet mentioned in the published reports. These estimates and, where reported, the percentage of the population with low serum zinc concentration, were compared (Appendix 2) and are summarized in **figure 8**.

For the few studies that have reported the prevalence of low serum zinc concentrations in the study population, some observations may be made. One study among Indian women reported that 41.5% of the women had serum zinc concentrations less than 70 μg/dL, the lower cutoff commonly used for morning fasting blood samples [64]. The mean zinc intake of this group was 6.0 mg/day, and 50% of the women were estimated to have inadequate zinc intakes. In a study among Canadian women consuming vegetarian diets, the mean zinc intake was 9.2 mg/day, and the corresponding EAR for low bioavailability diets is 7 mg/day [65]. Assuming a coefficient of variation of 25%, the proportion of these women with low intakes would be approximately 8%; it was reported that 14% of those women had serum zinc concentrations less than 70 μg/dL. One study of older men in California reported that the 25th percentile of serum zinc concentration was 73.8 μg/dL, close to the IZiNCG suggested lower cutoff for morning fasting samples (74 μg/dL) [66]. A mean zinc intake of 17.1 mg/day, including supplement use, would have predicted a prevalence of low zinc intakes of only about 5%. However, it is possible that with supplement use the true width of the zinc intake was much wider than assumed, and the prevalence of low intakes may have been underestimated.

Several studies among pregnant women reported the prevalence of women with serum zinc concentrations below cutoffs appropriate for the trimester of pregnancy. With the use of the same assumptions about the intake distribution, the estimated prevalence of low intakes was very similar to the prevalence of low serum zinc. For example, the predicted prevalence rates of about 41% for Malawian women [67] and about 35% for Egyptian women [68] were close to the 47% and 30% low serum zinc concentrations reported for these studies, respectively. Similarly, in a study of US women during pregnancy, with a somewhat higher mean zinc intake of 9.7 mg/day and a predicted prevalence of inadequate intakes of about 24%, the prevalence of low serum zinc was 13% [69]. Finally, a small study among US women with still higher mean zinc intakes predicting a prevalence of low intakes of about 7% reported that no women presented low serum zinc concentrations [37].

For lactating women, in one study with a mean intake level of 8.4 mg/day, with predicted prevalence of low intakes of about 24%, one of the seven participants

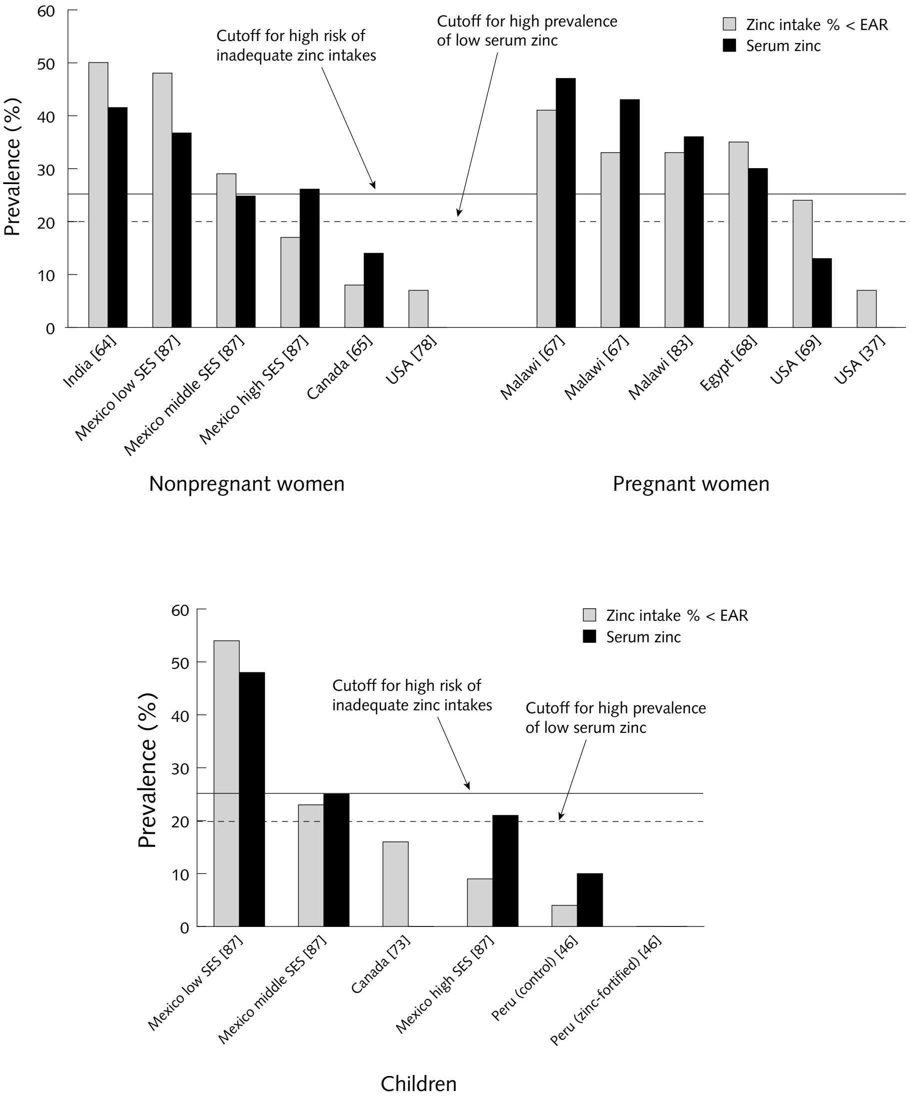

FIG. 8. Prevalence of low serum zinc concentration and inadequate zinc intakes among pregnant and nonpregnant women (upper panel) and children (lower panel) as estimated from previously published data. Details of the data sources are given in Appendix 2. SES, socioeconomic status; EAR, estimated average requirement

(14%) was reported to have low serum zinc [70].

For school-aged and preschool children, conformity is somewhat less consistent. In one study in Kenya, it was reported that 66% of a group of schoolchildren had low serum zinc [71]. The mean zinc intake was reported for children 6 to 14 years of age, which crosses two age groups for EARs, but the mean intakes reported were well above the EARs for the corresponding age groups, assuming low bioavailability. It is possible that chronic infection, including malaria, confounded the results in this population. Some of the data sets reported were from baseline data collected for zinc supplementation interventions in which a positive, linear growth response was observed among the children [72–75]. The Chilean study in schoolchildren would have predicted a 25% prevalence of low zinc intakes [72]. The Chilean study of preschool children would have predicted that no children would have low zinc intakes, thus conforming to the 0% prevalence of low serum zinc concentrations, but not explaining why a linear growth response was observed [75]. The study in Canadian schoolchildren would have predicted a prevalence of low intakes of about 15%; although no children had low serum zinc concentrations, all of them had low hair zinc concentrations (< 1.68 µmol/g) [73] and a positive growth response was observed. Only one of those three studies reported a high prevalence (39%) of low serum zinc [74], but based on the mean zinc intake in that study, 2% or less of the children would have had intakes below the EAR.

A longitudinal study conducted in a small number of Peruvian children showed that the group that received a non-zinc-fortified diet for 70 days had a mean zinc intake of 5.4 mg/day (EAR of 3 mg/day for moderate bioavailability diets) and 10% had low serum zinc [46]; in two other groups consuming the same diet but fortified with zinc to give mean intakes of 8.7 and 15.7 mg zinc/day, none had low serum zinc concentrations at the end of the intervention.

A national survey of British children was also conducted where usual zinc intakes from 7 days of weighed records were determined for children of various age ranges and for whom serum zinc concentration was determined in a subset [86] (Appendix 2). For most age and sex groups, both indicators predicted a low prevalence of risk of zinc deficiency of 10% or less, with the exception of preadolescent girls, who had a higher prevalence of low zinc intakes (32%). Nonetheless, the prevalence of low intakes used the British recommended nutrient intakes, which are higher than the IZiNCG EARs for diets of moderate bioavailability.

A national nutrition survey carried out in Mexico in 1999 included an estimate of bioavailable zinc intakes, as well as serum zinc concentrations in a subsample of participants. The amount of bioavailable zinc was estimated for each individual by the equation presented by IZiNCG, and the proportion of individuals with absorbed zinc intakes below the physiological requirement was determined, assuming the coefficient of variation of the intake distribution was 25% [87]. The proportion of children with serum zinc concentration below the age group-appropriate morning, nonfasting cutoff was compared by socioeconomic status terciles. The prevalence of low intake of bioavailable zinc predicted a similar magnitude of risk of zinc deficiency, as did the prevalence of low serum zinc concentrations for both preschool children and adolescent girls and women in Mexico [87], both at the national level and when stratified by socioeconomic status. Further, the suggested cutoffs for each indicator at which the risk of zinc deficiency is considered to be of public health concern (i.e., 25% prevalence of inadequate zinc intakes and 20% prevalence of low serum zinc concentrations) identify the same groups to be at elevated risk.

The prevalence rates of low serum zinc and inadequate zinc intakes estimated as described above for pregnant and nonpregnant women and children are presented graphically in **figure 8**. It is noteworthy that the suggested cutoffs of greater than 20% for low serum zinc and greater than 25% for inadequate zinc intakes (reference lines shown) would predict an elevated risk of zinc deficiency for Indian, Malawian, and Egyptian women, but not US or Canadian women. For children, these cutoffs would predict elevated risk of zinc deficiency among Mexican children of low socioeconomic status, and marginally among those of moderate socioeconomic status.

Despite the fairly crude assumptions about the distribution of zinc intakes in these populations and the limited amount of information available, there appears to be reasonable conformity between the predicted prevalence rates of zinc deficiency risk based on dietary and biochemical indicators among adults. The evidence for conformity among children is still very weak, perhaps because of the existence of many possible confounding factors not controlled for (e.g., infection), small sample sizes, and nonrepresentative selection of children to participate in studies, and also possibly because the dietary requirement estimates for children are less accurate because they were derived by extrapolation from adult studies. Unfortunately, most studies that have looked at functional responses to supplemental zinc have not included dietary assessments of usual zinc intakes.

Although there is some evidence for conformity of results for dietary and biochemical or functional indicators of zinc status, most studies have not presented data in a way that can adequately test the validity of adequacy of dietary zinc intake as an indicator of zinc status. Further studies of usual zinc intakes and biochemical and functional indicators of zinc status should be conducted among high-risk age groups in a variety of settings. Such studies must control for both past and present infections and should test the indicators presented in this review series with the use of appropriate cutoffs. Use of the 25% level for prevalence of inadequate intakes representing zinc deficiency also needs to be substantiated by further population-based studies.

Summary

New models for estimating physiological requirements for absorbed zinc and for estimating the percent absorption of dietary zinc from different diet types have been presented in recent years. The dietary requirements, thus derived, presented by IZiNCG represent the best possible estimates with available data and knowledge and are considered to be appropriate for international use. Information on zinc status of subjects participating in controlled, clinical studies of zinc intakes suggests that the physiological requirement estimates presented by IZiNCG are valid. Most reports from community-based studies of zinc intakes and other indicators of zinc status have not presented data in such a way that the validity of the EARs can be evaluated. Data from one National Nutrition Survey analyzed for this purpose suggest that the prevalence of inadequate intakes of bioavailable zinc, taken together with the prevalence of low serum zinc concentration, may be a good predictor of the risk of zinc deficiency at the population level. At least among adults, data from smaller studies indicate conformity in the prediction of the risk of zinc deficiency using the EAR cut-point method for adequacy of dietary zinc intakes and the proportion of individuals with serum zinc below the lower limit.

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Appendix 1

Biochemical and functional indicators of zinc status according to amount of absorbed zinc among adult men and women

Study diet	Reference	Zinc intake (mg/day)	Study duration (wk)	Phytate:zinc ratio	Absorbed zinc (mg/day)	Outcomes: biochemical (static tests)	Functional or biochemical functional tests	Zinc status
Adult men								
Depletion	[9]	0.28	4–9	0	0.3^a	Decreased plasma zinc; all < 70 µg/dL	Balance not achieved	Deficient
Depletion	[6]	0.9	3–4	0	0.8	Decreased serum zinc < 70.0 µg/dL; decreased erythrocyte zinc and urinary zinc	4/5 balance not achieved, 5th in balance but with clinical signs of zinc deficiency	Deficient
Depletion	[7]	1.43	5	1^a	1.0^a	7/9 serum zinc < 70 µg/dL; 1/9 < 74 µg/dL; decreased urinary zinc	Zero balance	Marginal
Depletion	[76]	4	6	58	1.1^a	Decreased plasma zinc but most above 74 µg/dL; decreased urinary zinc	Decreased taste acuity and cellular immune response	Marginal
Depletion	[7]	2.45	5	1^a	1.6^a	5/9 serum zinc < 70 µg/dL; 5/9 < 74 µg/dL; decreased urinary zinc	Zinc balance maintained	Marginal
Depletion	[7]	3.37	5	1^a	2.0^a	1/9 serum zinc < 70 µg/dL; 3/9 < 74 µg/dL; decreased urinary zinc	Zinc balance maintained	Marginal/ adequate
Depletion	[5]	3.6	17	1^a	2.1^a	Maintained serum zinc in normal range		Adequate
Depletion	[77]	3.8	9	1^a	2.2^a	Decreased serum zinc (mean, 71.2 µg/dL), erythrocyte zinc	Decreased erythrocyte carbonic anhydrase activity, increased ventilatory equivalents during exercise	Marginal
Depletion	[10]	4.1	24	21	2.4	Decreased serum zinc, but mean (105.5 µg/dL) well above cutoff); decreased white blood cell zinc	Balance NOT achieved in all subjects but near 0 (mean, –0.13 mg zinc/day)	Marginal/ adequate
Depletion	[7]	4.43	5	1^a	2.5^a	1/9 serum zinc < 70 µg/dL; 3/9 < 74 µg/dL; decreased urinary zinc	Zinc balance maintained	Marginal/ adequate
Depletion	[12]	15	2	15	2.63	Maintained serum zinc in normal range	0/4 achieved zinc balance	Adequate/ marginal
Depletion	[15]	5.5	7.7	4	2.8	Maintained serum, urinary zinc	5/6 achieved zinc balance	Adequate
Standard	[10]	12.6	4	5^a	5.5	Normal serum zinc		Adequate
Standard	[12]	15	2	0	5.1	Normal serum zinc		Adequate
Standard	[15]	16.5	1.7	1	5.9	Normal serum zinc, erythrocyte zinc, and carbonic anhydrase		Adequate

continued

Biochemical and functional indicators of zinc status according to amount of absorbed zinc among adult men and women *(continued)*

Study diet	Reference	Zinc intake (mg/day)	Study duration (wk)	Phytate:zinc ratio	Absorbed zinc (mg/day)	Outcomes: biochemical (static tests)	Functional or biochemical functional tests	Zinc status
Repletion	[77]	18.7		1^a	6.4^a	Normal serum zinc, erythrocyte zinc, and carbonic anhydrase		Adequate
Repletion	[76]	30	2	1	8.4^a	Increased plasma zinc and urinary zinc	Increased cellular immune response	Adequate
Adult women								
Depletion	[61]	2.64	24	1^a	1.6^a	Plasma zinc decreased but mean (84.6 µg/dL) remained > cutoff	Zinc balance marginal, probably negative	Marginal
Depletion	[62, 63]	3	13	1^a	1.8^a	Mean plasma zinc remained in normal range (mean, 876–96.7 µg/dL), superoxide dismutase decreased only when copper intake was low (1 mg/day) (both increased after supplementation)	Increased osteocalcin	Marginal/ adequate
Standard	[18]	7.8	7	5	2.3	Mean plasma zinc (75.8 µg/dL) > cutoff	Zinc balance marginal	Adequate/ marginal
Standard	[18]	14	7	5	3.1	Mean plasma zinc (74.5 µg/dL) > cutoff	Zinc balance maintained	Adequate
Standard	[17]	9.1	8	14	2.4	Mean plasma zinc (90.8 µg/dL) > cutoff	Zinc balance maintained	Adequate
Standard	[17]	11.1	8	5	3.7	Mean plasma zinc (96.1 µg/dL) > cutoff	Zinc balance maintained	Adequate

[a] The amount of absorbed zinc was estimated by the IZiNCG [4] algorithm using total zinc intake and total phytate:zinc molar ratio of the diet. The phytate:zinc molar ratio was assumed to be 1 for highly refined depletion diets or repletion diets with high levels of supplemental zinc; the phytate:zinc molar ratio was assumed to be 5 for refined, mixed diets when phytate content was not reported.

Appendix 2

Summary of studies that determined mean zinc intakes and mean serum zinc concentrations and/or other indicators of zinc status in groups

Source	Country	N[a]	Sex	Age (yr)	IZiNCG EAR (mg/day)	Bioavailability category	Mean zinc intake (mg/day)	% with inadequate zinc intakes[b]	Mean serum zinc (μg/dL)	% with low serum/plasma zinc	Other indicators of zinc status
Adult men											
[78]	USA	10	M	25–44	15	Low	12.2	82%	98.7		
[79]	India	904	M	25–64	10	Moderate	7.0	96%	90.7		
[79]	India	894	M	25–64	10	Moderate	8.8	71%	98.1		
[78]	USA	10	M	25–44	10	Moderate	15.0	9%	105.9		
[66]	USA	375	M	45–92	10	Moderate	17.1	5%	83.0	12.7% (range, 8.5%–20.4%)	25th percentile 73.8 μg/dL associated with lower bone mineral density
Adult women											
[78]	USA	15	F	25–44	7	Low	10.8	8%	89.5	0% had low serum zinc concentrations	
[65]	Canada	47	F		7	Low	9.2	17%	99.3	14% < 70 μg/dL (as reported)	
[79]	India	902	F	25–64	6	Moderate	5.6	61%	88.3		
[64]	India	258	F	18–23	6	Moderate	6.0	50%	74.2	41.5% < 70 μg/dL	
[80]	Chile	21	F	18–41	6	Moderate	6.7	34%	90.6		
[81]	USA	23	F	20–28	8	Moderate	7.1	69%	67.0		All used oral contraceptives
[79]	India	875	F	25–64	6	Moderate	8.1	15%	100.0		
[82]	USA	996	F	18–24	6	Moderate	8.1	15%		Reference population: theoretical 2.5% with low serum zinc	
[78]	USA	10	F	25–44	6	Moderate	13.2	1%	90.2		
Pregnant women											
[67]	Malawi	71	F		8	Moderate	8.7	37%	43.1	47% < 42.5 μg/dL	42% hair zinc < 1.68 μmol/g; presence of malaria
[68]	Egypt	50	F	17–36	8	Moderate	8.8	36%	65.4	30% < 55.5 μg/dL	

continued

Summary of studies that determined mean zinc intakes and mean serum zinc concentrations and/or other indicators of zinc status in groups *(continued)*

Source	Country	N^a	Sex	Age (yr)	IZiNCG EAR (mg/day)	Bioavail-ability category	Mean zinc intake (mg/day)	% with inadequate zinc intakes^b	Mean serum zinc (µg/dL)	% with low serum/plasma zinc	Other indicators of zinc status
[83]	Malawi	141	F	14–45	8	Moderate	9.0	33%	52.9	36% < 46.4 µg/dL	46% hair zinc < 1.68 µmol/g; presence of malaria
[67]	Malawi	69/65	F	14–45	8	Moderate	9.1	31%	51.6	43% < 46.4 µg/dL	32% hair zinc < 1.68 µmol/g; presence of malaria
[69]	USA	104	F	24.4 ± 5.3	8	Moderate	9.7	24%	65.7	13% < 53.3 µg/dL	
[37]	USA	9	F		8	Moderate	12.4	8%	60.8	None	
[84]	USA	244	F	22.8 ± 5.4	8	Moderate	13.2	6%	63.4	–	
Lactating women											
[70]	Brazil	7	F		7	Moderate	8.4	25%	87.1	14% ($N = 1$)	Women in apparent zinc balance
[35]	USA	9	F		7	Moderate	11.0	7%	85.6	0%	
[85]	USA	31	F		7	Moderate	12.6	4%	86.9		No change in milk zinc concentration after zinc supplementation
School-aged children											
[71]	Kenya	492	M/F	6 –14	4–7	Low	7–9			66%	19% stunted, 30% underweight; presence of malaria
[86]	Great Britain	207 (83)	F	7–10	5	Moderate	5.8	(9%)	96.1	1%	
[86]	Great Britain	228 (111)	M	7–10	5	Moderate	6.4	(4%)	98.7	1%	
[73]	Canada	30 (21)	M	5–7	5	Moderate	6.7	16%	101.9	0%	Boys with hair zinc < 1.68 µmol/g increased linear growth after zinc supplementation
[86]	Great Britain	209 (126)	F	11–14	5	Moderate	6.7	(32%)	97.4	2%	
[86]	Great Britain	212 (136)	M	11–14	5	Moderate	7.7	(12%)	95.4	0%	

[86]	Great Britain	183 (123)	F	15–18	7	Moderate	7.5	(9%)	92.1	5%	
[86]	Great Britain	163 (124)	M	15–18	8	Moderate	9.7	(8%)	96.7	2%	
Preschool children											
[58]	Malawi	50	M/F	3–6	2–4	Low	7.4		–		27% low hair zinc; 57% stunted
[86]	Great Britain	151 (30)	F	4–6	3	Moderate	5.0	(22%)	98.0	0%	
[58]	Ghana	67	M/F	3–6	3	Moderate	5.1	5%	–		8%–17% low hair zinc; 28% stunted
[46]	Peru	10	M/F	4	3	Moderate	5.4	4%	77.6	10%	
[86]	Great Britain	167 (34)	M	4–6	3	Moderate	5.6	(10%)	92.1	9%	
[74]	USA	20 (16)	M/F	2–6	2–3	Moderate	5.9	0%	70	39%	Increased linear growth after supplementation
[46]	Peru	9	M/F	4	3	Moderate	8.7	0%	76.2	0%	

IZiNCG EAR, International Zinc Nutrition Consultative Group estimated average requirement

a. *N* for dietary zinc (*N* for serum/plasma zinc).

b. Percentages in parentheses are estimates of the prevalence of inadequate intakes as presented in the original studies and determined from distributions of zinc intake adjusted for intraindividual variation.