Conclusions of the Joint WHO/UNICEF/IAEA/IZiNCG Interagency Meeting on Zinc Status Indicators

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Abstract

Zinc deficiency is an important cause of morbidity in developing countries, particularly among young children, yet little information is available on the global prevalence of zinc deficiency. A working group meeting was convened by the World Health Organization (WHO), the United Nations Children's Fund (UNICEF), the International Atomic Energy Agency (IAEA), and the International Zinc Nutrition Consultative Group (IZiNCG) to review methods of assessing population zinc status and provide standard recommendations for the use of specific biochemical, dietary, and functional indicators of zinc status in populations. The recommended biochemical indicator is the prevalence of serum zinc concentration less than the age/sex/time of day-specific cutoffs; when the prevalence is greater than 20%, intervention to improve zinc status is recommended. For dietary indicators, the prevalence (or probability) of zinc intakes below the appropriate estimated average requirement (EAR) should be used, as determined from quantitative dietary intake assessments. Where the prevalence of inadequate intakes of zinc is greater than 25%, the risk of zinc deficiency is considered to be elevated. Previous studies indicate that stunted children respond to zinc supplementation with increased growth. When the prevalence of low height-for-age is 20% or more, the prevalence of zinc deficiency may also be elevated. Ideally, all three types of indicators would be used together to obtain the best estimate of the risk of zinc deficiency in a population and to identify specific subgroups with elevated risk. These recommended indicators should be applied for national assessment of zinc status and to indicate the need for zinc interventions. The prevalence of low serum zinc and inadequate zinc intakes may be used to evaluate their impact on the target population's zinc status.

Key words: Diet, indicators, population, serum zinc, stunting, zinc

Introduction

Zinc deficiency is among the most important causes of morbidity in developing-country settings. There is an urgent need to begin to identify countries and regions that are at increased risk for zinc deficiency and to quantify the number of individuals at risk on a global scale. To date, there are very limited data available at the country level on the risk of zinc deficiency. In part, the assessment of zinc status may be hindered by the lack of standard, accepted guidelines on which indicators to use, how to carry out the assessment, and how to interpret the results.

A consultation workshop was convened by the World Health Organization (WHO), the International Atomic Energy Association (IAEA), and the United Nations Children's Fund (UNICEF) to review available indicators of population zinc status assessment and to present a set of recommendations to be adopted for international use. The three categories for population indicators considered were biochemical, dietary, and functional. Potential indicators for each category were reviewed and are presented in detail in the accompanying articles of this supplement. Recommendations were derived for the specific indicators to use and for appropriate cutoffs to interpret the level of risk of population zinc deficiency. The appropriateness of these indicators for monitoring the impact of zinc interventions was also considered. The recommendations from these papers and the consultation are summarized here.

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Biochemical indicators of zinc status

Biochemical indicators may be used as an objective and quantitative means of assessing the zinc status of a population. Such indicators can be useful for identifying populations and specific subgroups that are at elevated risk for zinc deficiency and may thus be used to identify groups to whom interventions should be targeted. Biochemical indicators may indicate the severity and extensiveness of zinc deficiency, although additional information will be needed as to the specific cause of the deficiency.

Basis for the selection of biomarkers of zinc status

Serum or plasma zinc is the best available biomarker of the risk of zinc deficiency in *populations*. The rationale for this selection is that serum or plasma zinc reflects dietary zinc intake; it responds consistently to zinc supplementation; and reference data are available for most age and sex groups. To date, serum zinc is the only biochemical indicator of zinc status known to meet these criteria.

It is recognized that serum zinc does not necessarily reflect *individual* zinc status or predict individual functional responses to supplementation; therefore, the use of this indicator for diagnosis and treatment of individuals is not recommended at this time. However, information on the distribution of serum zinc concentrations in a population will inform as to the magnitude of the risk of zinc deficiency at the population level.

Methodological considerations

Serum zinc concentration is affected by recent meals, time of day, age, sex, and systemic infections or inflammation. Therefore, these factors should be taken into account in the survey design and be adequately controlled for in analysis to correctly interpret results. Because samples are easily contaminated by ambient sources of zinc, appropriate care must be taken during collection, processing, and analysis of samples to avoid contamination. The sample included in the survey should be adequately representative of the population of interest.

Indicator for estimating the risk of zinc deficiency in a population

For population assessment, the recommended indicator to use is the percentage of the population with serum zinc concentrations below the age/sex/time of day-specific lower cutoff [1–3].

The recommended cutoffs are specific for age and sex groups as well as for the time of day of sampling and represent the 2.5th percentile of the serum zinc distribution from a healthy reference population [1]. The reference data used were derived from the National Health and Nutrition Examination Survey II and represent individuals more than 2 years of age. The recommended cutoff for children under 10 years of age is 65 µg/dL (9.9 µmol/L) for samples collected in the morning hours in a nonfasted state.

The risk of zinc deficiency is considered to be elevated and of public health concern when the prevalence of low serum zinc concentrations is greater than 20%. In this case, an intervention to improve population zinc status is recommended.

Indicator for monitoring or assessing the impact of interventions

The same indicator can be used to assess the impact of an intervention program by comparing the percentage of individuals with low serum zinc concentrations before and after initiation of the intervention.

Dietary indicators of the risk of zinc deficiency

The assessment of dietary zinc intakes at the population level is recommended for several reasons. It will provide information on the dietary patterns that may be associated with zinc adequacy or inadequacy and it can help to identify populations or subpopulations at elevated risk for inadequate zinc intakes.

Dietary intake information is necessary for the appropriate design of food-based interventions, including food fortification. In addition to identifying subpopulations at risk, it can be used to identify appropriate food vehicles to effect change in dietary zinc intakes (e.g., food vehicles for fortification) and to estimate the deficit in zinc intakes so that the amount of additional dietary zinc needed to meet population intake requirements can be estimated. Further, it is essential to measure the change in intake in response to any intervention aimed at improving zinc intake, especially fortification, as well as progress towards meeting dietary requirements.

The participants recognized that dietary assessment may not be used to define zinc status per se but rather the *risk* of zinc deficiency in a population. Stronger conclusions regarding the level of risk of zinc deficiency in a population, and hence the need for intervention, may be reached when dietary assessment is used in combination with biochemical indicators of zinc status, such as serum zinc.

Basis for the selection of dietary reference intake levels for zinc

Several expert committees have presented dietary reference intake levels for zinc in the last decade, and these were reviewed extensively [4]. The recommended intake levels that were based on the updated information and are most appropriate for international use were those presented by the International Zinc Nutrition Consultative Group (IZiNCG) [2]. It is thus recommended that WHO/FAO/IAEA review their current estimates in light of new scientific evidence so that a single set of internationally recognized dietary reference intakes for zinc can be established.

Methodological considerations

When considering resources and validity, the most appropriate dietary assessment method for use in surveys is the 24-hour recall. Ideally, more than one day of intake data would be collected for each individual in the sample, or for a subset of individuals, thus allowing for a better estimation of the distribution of zinc intakes in the population. It is recognized, however, that limitations in available resources may not always permit repeated recalls to be used.

Indicator for estimating the risk of zinc deficiency in a population

For population assessment, the specific indicator to be used is the prevalence of the population with zinc intakes below the estimated average requirement (EAR) *or* the probability of zinc intakes below the EAR. Before determining this prevalence, the width of the distribution of usual zinc intakes needs to be either corrected, based on data from the repeated recalls collected, or fixed, based on an assumed width of the distribution [4]. These are specific for age and physiological status groups and for two different diet types (mixed/refined vegetarian diets or unrefined cereal-based diets) defined by their phytate:zinc molar ratio.

The risk of zinc deficiency is considered to be elevated and of public health concern when the prevalence or probability of inadequate intakes is greater than 25%. In this case, an intervention to increase population dietary zinc intake is required.

Indicator for monitoring or assessing the impact of interventions

The same indicator can be used to assess the impact of food-based interventions by comparing the percentage of individuals with inadequate zinc intakes before and after initiation of the intervention.

Functional indicators of zinc status

Functional outcomes of nutritional deficiency states indicate that optimal health and biological function are impaired, and several such outcomes can be assessed by relatively rapid and noninvasive methods. Although a few functional indicators may be associated with zinc status, they are not specific to zinc status and may be associated with other nutritional deficiencies or the presence of infection. Also, although some infectious diseases are responsive to supplemental zinc, the prevalence of those diseases would also be modified by the level of exposure to the infectious agents. Therefore, functional indicators may be useful for identifying populations or subpopulations likely to be at elevated risk for zinc deficiency, but they would be of limited value in quantifying the prevalence of zinc deficiency in the population.

Basis for the selection of functional outcomes related to zinc status

Height- or length-for-age is the best-known functional outcome associated with the risk of zinc deficiency in populations [5]. The rationale for this selection is that low height- or length-for-age is often responsive to supplemental zinc; standardized methods to measure this outcome exist and are widely used; and reference data are available. This measure has the advantage that it is often included in national health and nutrition monitoring activities. Although the same may be said for weight-for-age as an indicator, height- or length-for-age is preferred because the linear growth is likely to be the primary response to increased zinc intake, whereas weight gain is likely to occur as a result of increased linear growth.

It is recognized that low height- or length-for-age is not specific to zinc deficiency and is limited to assessment in children. Other important functional outcomes that have also been shown to be responsive to supplemental zinc are more difficult to define in a standardized manner (e.g., diarrheal episodes).

Methodological considerations

Standardized methods for measuring length (in children under 2 years of age) and height (in children 2 years of age or older) are well established. The exact age of the child must be known and is ideally determined from birth certificates or other such written records of birth date.

Indicator for estimating the risk of zinc deficiency in a population

For population assessment, the recommended indicator to use is the percentage of children under 5 years of age with length- or height-for age less than –2.0 SD below the age-specific median of the reference population [6].

The age-specific reference data for height- or length-for-age distributions are those of the WHO/Centers for Disease Control and Prevention (CDC)/National Center for Health Statistics (NCHS).

The risk of zinc deficiency is considered to be of elevated public health concern when the prevalence of low height- or length-for-age is at least 20%. An intervention to improve population zinc status is recommended.

Indicator for monitoring or assessing the impact of interventions

Monitoring change in the prevalence of low height- or length-for-age may not be appropriate to evaluate programs designed to impact zinc status only, as many other limiting factors may intervene. However, as most zinc intervention activities would generally be linked with other nutrition and health interventions, this indicator should still be included as a general indicator of impact.

General issues for population zinc status assessment

Before designing a population zinc assessment and selecting appropriate indicators, it is important to define the overall objectives of the survey. These will influence the sampling strategy and the sample size. Subsamples should be selected that are representative of rural versus urban populations, different socioeconomic-status groups, high-risk groups such as young children and women of reproductive age, and other disadvantaged groups.

Ideally, all of the above indicators would be included in a survey to provide complementary information, thus strengthening conclusions regarding zinc status of the population and the need for intervention. It is unlikely that large-scale surveys would be implemented solely for the purpose of assessing zinc status. Rather, zinc status assessments would more likely to be included within general surveys of health and nutritional status. Therefore, the selection of indicators for assessing zinc status may partly be determined by the broader objectives of the survey. It is also recognized that resources for data collection will be limited in some situations, and only a selection of indicators may be included. A suggested approach to selecting indicators according to level of available resources is outlined in **table 1**.

As there is presently limited practical experience with large-scale assessments of population zinc status, these recommendations are based on existing knowledge largely derived from nonrepresentative population- or community-based studies. Opportunities to evaluate the validity of these indicators and cutoffs should be sought. As more experience is gained, these recommendations should be reviewed and refined as necessary.

Research recommendations

In addition to research linked to the evaluation of population-based zinc intervention programs using the recommended indicators, other specific research priorities were identified.

Basic research to refine the reference data used for interpretation of population zinc status should include:

Table 1. Suggested approach to assessing zinc status of a population according to level of resources available

Limited resources available	Review existing evidence: Stunting rates (low height- or length-for-age) of children under 5 years of age; Dietary patterns and likelihood of providing adequate bioavailable zinc in the food supply; Results from clinical, community-based studies of functional response to zinc supplements; Results from community-based studies on dietary zinc intakes or serum zinc concentration
Some resources available	Augment existing information with data collected in a prospective survey. This would normally be linked with other health/nutrition surveys with broader goals: In at least a subsample of the survey population, or samples focused among subpopulations that are likely beneficiaries of nutrition or health interventions, include serum zinc concentration and/or dietary zinc intake adequacy as indicators; Where food-based interventions may be considered, at least 1 day of 24-hour recall per individual in the sample should be completed
Adequate resources available	Where resources permit: Serum zinc concentration should be determined in a representative sample of all relevant subpopulation groups; 24-hour dietary recalls, or other locally validated quantitative dietary assessment methods, would be repeated on nonconsecutive days to estimate the distribution of usual zinc intakes

- Direct study of zinc requirements in children of different ages using isotopic techniques;
- Direct study of zinc absorption among children from a variety of typical diets using isotopic techniques and, among adults and children, further studies of zinc absorption from diets with a high phytate:zinc molar ratio;
- Identification of new, sensitive and specific biochemical indicators of zinc status.

To gain a better understanding of how the recommended indicators for assessing population zinc status are interrelated, and to assess their validity, priority areas of research include:

- Analysis of existing or prospectively collected cross-sectional data on serum zinc and dietary zinc intakes from population-based surveys to determine whether these indicators are associated with one another;
- Determining the response of plasma zinc and functional indicators of zinc status to food-based interventions that alter the adequacy of dietary zinc intakes (e.g., food fortification, dietary modification, biofortification).

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