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Nutritional care and support for patients with tuberculosis: A review on guidelines issued by WHO

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ABSTRACT

The aim of this guideline is to help improve health outcomes for people with tuberculosis (TB), through improved nutritional care and support. The objectives of the guideline, to provide guidance on nutritional assessment, advice and treatment, for integration into clinical care for people with TB. Five guiding principles for nutritional care and support for people with TB are presented. The focus is on nutrition assessment, counseling and management to improve the clinical care of people with TB. These should be considered an essential part of services for people with TB and can be adapted according to countries' burden of disease and healthcare infrastructure, including human resource capacity. It is recognized that food assistance1 is sometimes used in TB programs for purposes other than nutritional care, especially in food-insecure settings. Specific guidance regarding the role of food assistance as part of a larger package of services intended to improve access and adherence to treatment and to mitigate the financial and social consequences of TB will be addressed elsewhere. The primary audience for the guideline is health workers providing care to people with TB. However, the guideline is also intended for a wide audience, including policy makers, their expert advisers, and technical and program staff managing national and subnational TB programs and nongovernmental agencies that deliver TB services, and for policy-makers involved with scaling up TB prevention, diagnosis and treatment, including adherence to and completion of therapy.

Keywords: Nutritional, Care, Support, Tuberculosis, Guidelines, WHO

INTRODUCTION

WHO has issued the guideline for nutritional care and support for patients with tuberculosis in November 2013. This guideline provides guidance on the principles and evidence-informed recommendations on the nutritional care and support for patients with tuberculosis. Under-nutrition increases the risk of tuberculosis (TB) and in turn TB can lead to malnutrition. Under nutrition is therefore highly prevalent among people with TB. It has been demonstrated that under-nutrition is a risk factor for progression from TB infection to active TB disease and that under-nutrition at the time of diagnosis of active TB is a predictor of increased risk of death and TB relapse. However, the evidence concerning the effect of nutritional supplementation on TB prevention and health outcomes among people with TB had not previously been systematically reviewed. This guideline provides guidance on the principles and recommendations for nutritional care and support of patients with TB as part of their regular TB care. However, it does not consider the provision of food as part of a package of enablers to improve TB treatment adherence or as means to mitigate the negative financial consequences of TB. Member States have requested guidance from the World Health Organization (WHO) on nutritional care and support for patients with TB, in support of their efforts to achieve the Millennium Development Goals. The primary audience for the guideline is health workers providing care to people with TB. However, the guideline is also intended for a wider audience, including policy-makers, their expert advisers, and technical and programme staff at organizations involved in the design, implementation and scaling-up of nutrition actions for public health.

PRINCIPLES

Five guiding principles[1] are key for providing nutritional care and support as an integral part of TB care and prevention.

1. All people with active TB should receive TB diagnosis, treatment and care according to WHO guidelines and international standards of care. When malnutrition is identified at the time of TB diagnosis, TB is considered a key causal factor that needs to be addressed. It is essential that nutrition assessment and assistance do not divert resources from optimal TB diagnosis and care. Concerns about weight loss or failure to gain weight during TB treatment should trigger further clinical assessment (e.g. resistance to TB drugs, poor adherence, comorbid conditions) and nutrition assessment of the causes of under-nutrition, in order to

determine the most appropriate interventions.

2. An adequate diet, containing all essential macro- and micronutrients, is necessary for the well-being and health of all people, including those with TB infection or TB disease.

3. Because of the clear bidirectional causal link between under-nutrition and active TB, nutrition screening, assessment and management are integral components of TB treatment and care.

4. Poverty and food insecurity are both causes and consequences of TB, and those involved in TB care therefore play an important role in recognizing and addressing these wider socioeconomic issues.

5. TB is commonly accompanied by comorbidities such as HIV, diabetes mellitus, smoking and alcohol or substance abuse, which have their own nutritional implications, and these should be fully considered during nutrition screening, assessment and counselling.

SCOPE OF THE GUIDELINE, EVIDENCE APPRAISAL AND DECISION-MAKING

Since there were no internationally agreed recommendations on what nutrition care or food assistance TB patients should receive, or on how national TB programmes can contribute to improving a population's nutritional status, the Department of Nutrition for Health and Development and the Global TB Programme (GTB) planned to develop such recommendations and guidelines jointly. A scoping meeting for the development of recommendations on nutritional support/food assistance to prevent TB and improve health status among TB patients was held in Geneva, 2–4 November 2009 [60]. An initial set of questions (and the components of the questions) to be addressed in the guideline was the critical starting point for formulating the recommendation. The questions were drafted by technical staff at the Evidence and Programme Guidance Unit, Department of Nutrition for Health and Development, and the Policy, Strategy and Innovations unit, Global TB Programme, based on policy and programme guidance needs of Member States and their partners. The population, intervention, control, outcomes (PICO) format was used (Annex 3). The questions were discussed and reviewed by the WHO Steering Committee for Nutrition Guidelines Development, and feedback was received from five stakeholders. A Nutrition Guidance Advisory Group

meeting was held on 16–18 November 2010 in Amman, Jordan, to finalize the scope of the questions and rank the critical outcomes and populations of interest. The guideline development group discussed the relevance of the questions and modified them as needed. The guideline group scored the relative importance of each outcome.

The final key questions on this intervention, along with the outcomes were identified as critical and important for decision-making. One Cochrane1 review [27] and two supplementary reviews were used to summarize and appraise the evidence [62, 63]. WHO technical staff, together with methods experts of the guideline group, prepared evidence summaries according to the Grading of Recommendations Assessment, Development and Evaluation *(64)* (GRADE) approach to assess the overall quality of the evidence *(65)*. Both the systematic reviews and the GRADE evidence profiles for each of the critical outcomes were used for drafting this guideline. However, GRADE tables were only developed for those questions for which there were published studies included in the reviews. Some recommendations were developed based on recommendations previously made by WHO on nutritional care and support. The draft recommendation was discussed by the WHO Steering Committee for Nutrition Guidelines Development and the guideline development group, at a second guideline development consultation, held in Geneva between 28 November and 1 December 2011. The procedures for decision-making were established at the beginning of the meetings, including a minimal set of rules for agreement and voting. At least two thirds of the guideline development group had to be present for an initial discussion of the evidence and proposed recommendation and remarks. The guideline development group secretly voted on the direction and strength of the recommendation, using a form designed for this purpose, which also included a section for documenting their views on (i) the desirable and undesirable effects of the intervention; (ii) the quality of the available evidence; (iii) values and preferences related to the intervention in different settings; and (iv) the cost of options available to health-care workers in different settings.

Each member had one vote if not advised otherwise, after managing any potential conflict of interests. Abstentions were not allowed. The WHO Secretariat collected the forms and disclosed the summary of the results to the guideline development group. If there was no unanimous consensus, more time was given for deliberations and a second round

of voting was possible. If there was no full agreement, a two thirds vote of the guideline development group would have been required for the approval of the proposed recommendation. Divergent opinions, if any, were recorded in the guideline. Voting forms will be kept on file by WHO for 10 years. Consensus was reached for all recommendations. WHO staff present at the meeting, as well as other external technical experts involved in the collection and grading of the evidence, were not allowed to vote. There were no strong disagreements among the guideline group members. A draft of the revised principles and recommendations was disseminated for external peer review in February 2012.

Reviewers were asked to examine the principles and recommendations, to ensure that there were no important omissions, contradictions or inconsistencies with scientific evidence or programmatic feasibility; and to assist with clarifying the language, especially in relation to implementation and how policy-makers and programme staff might read them. Reviewers were advised that no additional recommendations could be considered and that they were being asked to undertake this exercise in their personal capacity and not as representatives of any agency or institution. External reviewers proposed several comments to make the recommendations clearer. There was no major disagreement. The draft principles and recommendations were circulated to all involved WHO technical staff; all TB regional advisers in all WHO regional offices; selected national TB programmes; several technical agencies working on TB control, including KNCV Tuberculosis Foundation, the Centers for Disease Control and Prevention and the International Union Against TB and Lung Disease; and a network of external experts for TB and nutrition, respectively. All interested stakeholders became members of the external experts' and stakeholders' panel but were only allowed to comment on the draft guideline after submitting a signed declaration of interests form. Feedback was received from these stakeholders. WHO staff addressed each comment and then finalized the guideline and submitted it for clearance by WHO before publication.

Key principles

The Nutrition Guidance Advisory Group agreed on five key guiding principles[1] that should be considered together with the evidence-informed recommendations. The principles are intended to inform and assist national technical groups, international and regional partners providing TB care, TB treatment

services, and/or maternal and child health services in countries affected by TB, in formulating national or subnational nutritional recommendations.

Key principle 1. All people with active TB should receive TB diagnosis, treatment and care according to WHO guidelines and international standards of care Appropriate diagnostic procedures, support for TB patients to complete treatment, and an appropriate combination of TB medications is crucial for curing the disease. The Stop TB Strategy provides the goals, objectives and indicators for TB care and control *(68)*. The *International Standards for Tuberculosis Care* is a widely accepted level of care that all practitioners should achieve in managing patients who have TB *(69)*. All essential elements of TB diagnosis and treatment should be provided free of charge to patients, in order to improve access to treatment and minimize the financial burden of the TB treatment on patients and households. When under-nutrition is identified at the time of TB diagnosis, TB should be considered a key causal factor that needs to be addressed. It is essential that nutrition assessment and assistance do not divert resources from optimal TB diagnosis and care.

Key principle 2. An adequate diet, containing all essential macro- and micronutrients, is necessary for the well-being and health of all people, including those with TB infection or TB disease Consuming a well-balanced and adequate diet is key to maintaining optimal health and physical function at all ages. Nutritional status is an important determinant of resistance to infection and of general well-being. It is well established that nutritional deficiency is associated with impaired immunity. While malnutrition increases susceptibility to infection, infection can lead to metabolic stress and weight loss, further weakening immune function and nutritional status *(13)*. Vitamins A, C, D, E, B6 and folic acid and the minerals zinc, copper, selenium and iron all play key roles in metabolic pathways, cellular function and immune function. The concentration of these nutrients may have a role in an individual's defence against TB *(13, 70)*. Under-nutrition is a strong contributor for active TB worldwide, and reduction in under-nutrition in the general population could dramatically reduce the incidence of TB *(11)*.

Key principle 3. Because of the clear bidirectional causal link between under-nutrition and active TB, nutrition screening, assessment and management are integral components of TB treatment and care Many people diagnosed with TB are undernourished at the time of diagnosis and nutrition intervention and care begin

with a nutrition assessment. Nutrition assessment (anthropometric,1 biochemical,2 clinical and dietary) is a prerequisite for the provision of good nutritional care. The results from screening and assessment inform counselling, which is usually done at the time of diagnosis and throughout treatment. Trained primary and lay health-care workers in primary and community health care can play an effective and integral role in nutrition screening and can identify patients affected by under-nutrition and in need of further assessment. *At diagnosis*, nutrition screening and assessment should include anthropometric and clinical measurements. If under-nutrition is diagnosed, dietary assessment is also indicated. The following are required:

• age-appropriate anthropometric measurements and classification of nutrition status *(71–75)*: u height and weight: o in children who are less than 5 years of age, determination of weight-for-length or weight-for-height Z-score, using the WHO child growth standards *(74)* o in children and adolescents aged 5–19 years, determination of BMI for-age-and-sex Z-score, using the WHO growth reference data for 5–19 years *(15, 74)* o in adults over 18 years of age, determination of BMI u mid-upper arm circumference: o in children who are less than 5 years of age and pregnant women.

• History of weight loss and signs of under-nutrition, such as visible wasting or oedema

• Clinical assessment for comorbid conditions and concurrent treatments

• Diet assessment if nutritional status indicates malnutrition. *At TB follow-up*, assessment should include, at a minimum:

• Anthropometric measures of weight, calculation of BMI and determination of weight and BMI change since diagnosis or last visit

• Classification of nutrition status *(71–75)*. In patients classified as having moderate under-nutrition, or severe acute malnutrition, further risk factor and dietary assessment will be necessary, such as: • poor TB treatment adherence and/or response, resistance to TB drugs

• Clinical assessment for other non-dietary causes of malnutrition, including identification of important comorbidities like HIV, diabetes mellitus or alcohol or drug abuse

• Biochemical assessment where possible dietary assessment, including assessment of food security. Weight loss or failure to regain or maintain a healthy weight, at any stage of disease should trigger further assessment and appropriate interventions. Weight status is particularly important for people with MDR-TB, who require a very

long duration of treatment and are more likely to require chronic care and palliative care. The goal of nutrition counselling is to improve the dietary intake during recovery, to compensate for the increase in energy expenditure associated with recovery and weight regain; support the increase in cellular production and immune responses; support repair of damaged and diseased tissues *(76)*; and manage the symptoms and side-effects of TB drugs, such as nausea and vomiting, anorexia, diarrhea and altered taste. Practical ways to meet macro- and micronutrient requirements through locally available and culturally appropriate foods should be provided.

Key principle 4. Poverty and food insecurity are both causes and consequences of TB, and those involved in TB care therefore play an important role in recognizing and addressing these wider socioeconomic issues Food insecurity, which is common in TB patients, and concomitant poor nutritional status, contribute to the global burden of active TB. As an integral part of TB care and control, the health sector should recognize and help address generalized malnutrition, food insecurity and other socioeconomic determinants and consequences of TB. Food insecurity can contribute to poor access and adherence to TB treatment. Although evidence for the positive impact of food intervention on access and adherence to TB treatment is currently limited, interventions that address food security have the potential to improve access and adherence to TB treatment, as well as to support nutritional recovery through provision of nutritious foods. Such interventions can also help mitigate some of the financial and social consequences of TB. While food and nutrition are essential to the health and well-being of all individuals, food assistance may be neither the best or most appropriate enabler for access and adherence to TB treatment, nor the best way to alleviate the catastrophic economic and social costs of TB. It is important to consider the context. Where access and adherence are suboptimal, the causes, including food insecurity, can be assessed and addressed with a suitable package of enablers, which may include food assistance. The health sector and TB programmes can link with food security programmes and the social protection services to ensure that those with active TB, and their families, have access to existing systems for adequate food assistance and social benefits. TB programmes can assess and minimize unnecessary costs to the patient, in order to minimize the economic and social consequences for those affected.

Key principle 5. TB is commonly accompanied by comorbidities such as HIV, diabetes mellitus, smoking and alcohol or substance misuse, which have their own nutritional implications, and these should be fully considered during nutrition screening, assessment and counselling Addressing comorbid conditions is of value not only for their potential contribution to nutritional status but also for improving access and response to TB treatment. Comorbid conditions should be considered as a part of a comprehensive clinical package for people with TB and/or under-nutrition, the aim of which should be to improve general health and quality of life. Nutritional counselling, advice and support may have to be adjusted to the specific nutritional requirements of other comorbid conditions. The immunosuppression associated with HIV has increased the incidence of active TB, especially in Africa where latent TB is common and HIV prevalence is high *(19)*. HIV also increases the risk of reactivation of TB and the risk of under-nutrition *(19)*. Guidance is available for nutritional care and support for people living with HIV/AIDS *(77)*. The increasing prevalence of diabetes mellitus in low- and middle-income countries is contributing to the sustained high incidence of TB disease. Diabetes mellitus triples the risk of developing TB and can worsen the clinical course of TB. TB can make management of blood glucose more difficult. Therefore, individuals with both TB and diabetes mellitus require careful clinical care.

Recommendations

Nutrition assessment and counselling • All individuals with active TB should receive

(i) an assessment of their nutritional status and

(ii) appropriate counselling based on their nutritional status at diagnosis and throughout treatment (strong recommendation, no evidence).

Management of severe acute malnutrition • School-age children and adolescents (5 to 19 years), and adults, including pregnant and lactating women, with active TB and severe acute malnutrition should be treated in accordance with the WHO recommendations for management of severe acute malnutrition *(2)* (strong recommendation, very low quality evidence). • Children who are less than 5 years of age with active TB and severe acute malnutrition should be treated in accordance with the WHO recommendations for the management of severe acute malnutrition in children who are less than 5 years of age *(3)* (strong recommendation, very low quality evidence).

Management of moderate under-nutrition

• School-age children and adolescents, and adults, including lactating women, with active TB and moderate under-nutrition, who fail to regain normal BMI after two months' TB treatment, as well as those who are losing weight during TB treatment, should be evaluated for adherence and comorbid conditions. They should also receive nutrition assessment and counselling, and, if indicated, be provided with locally available nutrient-rich or fortified supplementary foods, as necessary to restore normal nutritional status *(2)* (conditional recommendation, low quality evidence). • Children who are less than 5 years of age with active TB and moderate under-nutrition should be managed as any other children with moderate under-nutrition. This includes provision of locally available nutrient-rich or fortified supplementary foods, in order to restore appropriate weight-for-height *(4)* (strong recommendation, very low quality evidence). • Pregnant women with active TB and moderate under-nutrition, or with inadequate weight gain, should be provided with locally available nutrient-rich or fortified supplementary foods, as necessary to achieve an average weekly minimum weight gain of approximately 300 g in the second and third trimesters (strong recommendation, very low quality evidence). • Patients with active MDR-TB and moderate under-nutrition should be provided with locally available nutrient-rich or fortified supplementary foods, as necessary to restore normal nutritional status (strong recommendation, very low quality evidence).

Micronutrient supplementation

• A daily multiple micronutrient supplement at 1× recommended nutrient intake should be provided in situations where fortified or supplementary foods should have been provided in accordance with standard management of moderate under-nutrition *(2, 4)*, but are unavailable (conditional recommendation, very low quality evidence).

• All pregnant women with active TB should receive multiple micronutrient supplements that contain iron and folic acid and other vitamins and minerals, according to the United Nations Multiple Micronutrient Preparation *(5)*, to complement their maternal micronutrient needs (conditional recommendation, very low quality evidence).

• For pregnant women with active TB in settings where calcium intake is low, calcium supplementation as part of antenatal care is recommended for the prevention of pre-eclampsia, particularly among those pregnant women at higher risk of developing hypertension, in

accordance with WHO recommendations *(6, 42)* (strong recommendation, moderate quality evidence).

• All lactating women with active TB should be provided with iron and folic acid and other vitamin and minerals, according to the United Nations Multiple Micronutrient Preparation *(5)*, to complement their maternal micronutrient needs (conditional recommendation, very low quality evidence).

Contact investigation

• In settings where contact tracing is implemented, household contacts of people with active TB should have a nutrition screening and assessment as part of contact investigation. If malnutrition is identified, it should be managed according to WHO recommendations (*2–4*) (conditional recommendation, very low quality evidence).

Conclusion

• Nutritional assessment is an essential prerequisite to the provision of nutritional care. • There is no evidence to recommend that nutritional management of severe acute malnutrition should be different for those with active TB than for those without active TB. • There is no evidence to recommend that nutritional management of severe acute malnutrition should be different in children with active TB than for those without active TB. • Concerns about weight loss or failure to gain weight should trigger further clinical assessment (e.g. resistance to TB drugs, poor adherence, comorbid conditions) and nutrition assessment of the causes of under-nutrition, in order to determine the most appropriate interventions.

Closer nutritional monitoring and earlier initiation of nutrition support (before the first 2 months of TB treatment are completed) should be considered if the nutritional indicator is approaching the cut-off value for a diagnosis of severe acute malnutrition. • There is no evidence to recommend that nutritional management of moderate under-nutrition should be different for children (less than 5 years of age) with active TB than for those without. • Efforts should be made, within the sound principles of nutrition assessment, counselling and support, to ensure that TB patients are receiving the recommended intake of micronutrients, preferably through food or fortified foods. If that is not possible, micronutrient supplementation at 1× the recommended nutrient intake is warranted. • There is insufficient evidence to recommend that antenatal supplementation of calcium, iron and folic acid should be any different for pregnant women with active TB than for those without TB. However, since pregnant and lactating women with HIV

have improved maternal and birth outcomes when taking a multiple micronutrient supplement, pregnant women with TB were considered comparable to those with HIV in their potential benefit from having a multiple micronutrient supplement. • If pregnant or lactating women with moderate under-nutrition are receiving a fortified supplementary food product, then the micronutrient content of this product will have to be taken into account when considering a multiple micronutrient supplement, in order to avoid over-supplementation of micronutrients. • Screening for malnutrition, especially in children who are less than 5 years of age, is recommended at all health-care encounters and this should include contact investigation of TB.

References

1. WHO handbook for guideline development. Geneva: World Health Organization; 2012
2. IMAI district clinician manual: hospital care for adolescents and adults. Guidelines for the management of common illnesses with limited resources, volumes 1 and 2. Geneva: World Health Organization; 2011 (http://www.who.int/hiv/pub/imai/imai2011/en/, accessed 3 September 2013).
3. Guideline: Updates on the management of severe acute malnutrition in infants and children. Geneva: World Health Organization; 2013.
4. Technical note: Supplementary foods for the management of moderate acute malnutrition in infants and children 6–59 months of age. Geneva: World Health Organization; 2012 (http://www.who.int/nutrition/publications/moderate_malnutrition/9789241504423/en/index.html, accessed 3 September 2013).
5. 5. United Nations Children's Fund, World Health Organization, United Nations University. Composition of a multi-micronutrient supplement to be used in pilot programmes among pregnant women in developing countries: report of a United Nations Children's Fund (UNICEF), World Health Organization (WHO), United Nations University (UNU) workshop. New York: United Nations Children's Fund; 2000 (http://apps.who.int/iris/handle/10665/75358, accessed 3 September 2013).
6. 6. Guideline: Calcium supplementation in pregnant women. Geneva: World Health Organization;

2013 (http://apps.who.int/iris/bitstream/10665/85120/1/9789241505376_eng.pdf, accessed 3 September 2013).

7. Global tuberculosis report 2013. Geneva: World Health Organization; 2013.
8. Lönnroth K et al. Tuberculosis control and elimination 2010–50: cure, care, and social development. Lancet, 2010; 375:1814–29. doi: 10.1016/S0140-6736(10)60483-7.
9. Zachariah R, Spielmann MP, Harries AD, Salanipont FM. Moderate to severe malnutrition in patients with tuberculosis is a risk factor associated with early death. Trans. R. Soc. Trop. Med. Hyg. 2002;96:291–4.
10. Cegielski JP, McMurray DN. The relationship between malnutrition and tuberculosis: evidence from studies in humans and experimental animals. Int. J. Tuberc. Lung Dis. 2004;8:286–98.
11. Lönnroth K, Williams BG, Cegielski P, Dye C. A consistent log-linear relationship between tuberculosis incidence and body mass index. Int. J. Epidemiol. 2010; 39:149–55. doi: 10.1093/ije/dyp308.
12. Van Lettow M et al. Malnutrition and the severity of lung disease in adults with pulmonary tuberculosis in Malawi. Int. J. Tuberc. Lung Dis. 2004;8:211–7.
13. Papathakis P, Piwoz E. Nutrition and tuberculosis: a review of the literature and considerations for TB control programs. USAID/Africa's Health for 2010. Washington DC: Agency for International Development; 2008 (http://pdf.usaid.gov/pdf_docs/PNADL992.pdf, accessed 3 September 2013).
14. The influence of nutrition on the risk and outcomes of tuberculosis. In: HIV/AIDS, TB, and nutrition: scientific inquiry into the nutritional influences on human immunity with special reference to HIV infection and active TB in South Africa. Pretoria: Academy of Science of South Africa; 2007:153–72. (http://www.nationalacademies.org/asadi/PDFs/HIVAIDSTB&Nutrition.pdf, accessed 3 September 2013).
15. Management of severe malnutrition: a manual for physicians and other senior health workers. Geneva: World Health Organization; 1999 (http://www.who.int/nutrition/publications/severemalnutrition/9241545119/en, accessed 3 September 2013).
16. Dodor E. Evaluation of nutritional status of new tuberculosis patients at the effia-nkwanta regional hospital. Ghana Med. J. 2008;42(1): 22–8

(http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2423338/, accessed 3 September 2013).

17. Ramakrishnan CV, Rajendran K, Jacob PG, Fox W, Radhakrishna S. The role of diet in the treatment of pulmonary tuberculosis. An evaluation in a controlled chemotherapy study in home and sanatorium patients in South India. Bull. World Health Organ. 1961;25:39–59 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2555577/pdf/bullwho00319-0062.pdf, accessed 3 September 2013).
18. Vijayamalini M, Manoharan S. Lipid peroxidation, vitamins C, E and reduced glutathione levels in patients with pulmonary tuberculosis. Cell Biochem. Funct. 2004;22(1):19–22.
19. Semba RD, Darnton-Hill I, de Pee S, Addressing tuberculosis in the context of malnutrition and HIV coinfection. Food Nutr. Bull. 2010;31:S345–64.
20. van Lettow M et al. Micronutrient malnutrition and wasting in adults with pulmonary tuberculosis with and without HIV co-infection in Malawi. BMC Infect. Dis. 2004; 4(1):61. doi:10.1186/1471-2334-4-61.
21. Wilkinson RJ et al. Influence of vitamin D deficiency and vitamin D receptor polymorphisms on tuberculosis among Gujarati Asians in west London: a case-control study. Lancet. 2000; 355:618–21.
22. Metcalfe N. A study of tuberculosis, malnutrition and gender in Sri Lanka. Trans. R. Soc. Trop. Med. Hyg. 2005;99(2):115–9.
23. Podewils LJ et al. Impact of malnutrition on clinical presentation, clinical course, and mortality in MDR-TB patients. Epidemiol. Infect. 2011; 139:113–20. doi: 10.1017/S0950268810000907.
24. Hanrahan CF et al. Body mass index and risk of tuberculosis and death. AIDS, 2010;24(10):1501–8. doi: 10.1097/QAD.0b013e32833a2a4a.
25. Khan A, Sterling TR, Reves R, Vernon A, Horsburgh CR. Lack of weight gain and relapse risk in a large tuberculosis treatment trial. Am. J. Respir. Crit. Care Med. 2006; 174(3): 344–8. doi: 10.1164/rccm.200511- 1834OC.
26. Krapp F, Véliz JC, Cornejo E, Gotuzzo E, Seas C. Bodyweight gain to predict treatment outcome in patients with pulmonary tuberculosis in Peru. Int. J. Tuberc. Lung Dis. 2008; 12(10):1153–9.
27. Sinclair D, Abba K, Grobler L, Sudarsanam TD. Nutritional supplements for people being treated for active tuberculosis. Cochrane

Database Syst. Rev. 2011; (11):CD006086. DOI: 10.1002/14651858.CD006086.pub3.

28. Institute of Medicine. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC: National Academies Press; 2005 (http://www.nap.edu/openbook.php?isbn=0309085373, accessed 3 September 2013)

29. Ramakrishnan K, Shenbagarathai R, Kavitha K, Uma A, Balasubramaniam R, Thirumalaikolundusubramanian P. Serum zinc and albumin levels in pulmonary tuberculosis patients with and without HIV. Jpn. J. Infect. Dis. 2008;61(3):202–4.

30. Seyedrezazadeh E, Ostadrahimi A, Mahboob S, Assadi Y, Ghaemmagami J, Pourmogaddam M. Effect of vitamin E and selenium supplementation on oxidative stress status in pulmonary tuberculosis patients. Respirology, 2008; 13(2):294–8. doi: 10.1111/j.1440-1843.2007.01200.x.

31. Kassu A. et al. Alterations in serum levels of trace elements in tuberculosis and HIV infections. Eur. J. Clin. Nutr. 2006; 60(5):580–6. doi:10.1038/sj.ejcn.1602352.

32. Pakasi TA et al. Vitamin A deficiency and other factors associated with severe tuberculosis in Timor and Rote Islands, East Nusa Tenggara Province, Indonesia. Eur. J. Clin. Nutr. 2009;63(9):1130–5. doi: 10.1038/ ejcn.2009.25.

33. Kemp JR, Mann G, Simwaka BN, Salaniponi FM, Squire SB. Can Malawi's poor afford free tuberculosis services? Patient and household costs associated with a tuberculosis diagnosis in Lilongwe. Bull. World Health Organ. 2007;85(8):580–5. doi:10.2471.BLT.06.033167.

34. Siza JE. Risk factors associated with low birth weight of neonates among pregnant women attending a referral hospital in northern Tanzania. Tanzan. J. Health Res. 2008;10(1):1–8.

35. Figueroa-Damian R, Arredondo-Garcia JL. Neonatal outcome of children born to women with tuberculosis. Arch. Med. Res. 2001;32(1):66–9.

36. Jana N, Vasishta K, Saha SC, Ghosh K. Obstetrical outcomes among women with extrapulmonary tuberculosis. N. Engl. J. Med. 1999; 341(9):645–9. doi: 10.1056/NEJM199908263410903.

37. Kothari A, Mahadevan M, Girling J. Tuberculosis and pregnancy--Results

of a study in a high prevalence area in London. Eur. J. Obstet. Gynecol. Reprod. Biol. 2006;126(1):48–55.

38. Jana N, Vasishta K, Jindal SK, Khunnu B, Ghosh K. Perinatal outcome in pregnancies complicated by pulmonary tuberculosis. Int. J. Gynaecol. Obstet. 1994;44(2):119–24.

39. Heywood S., Amoa BM, Mola GL, Klufio CA. A survey of pregnant women with tuberculosis at the Port Moresby General Hospital. P. N. G. Med. J. 1999;42(3–4):63–70.

40. Bjerkedal T, Bahna SL, Lehmann EH. Course and outcome of pregnancy in women with pulmonary tuberculosis. Scand. J. Respir. Dis. 1975;56(5):245–50.

41. Nhan-Chang CL,Jones TB. Tuberculosis in pregnancy. Clin. Obstet. Gynecol. 2010;53(2):311–21.

42. WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia. Geneva: World Health Organization; 2011 (http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/9789241548335/en/index.html, accessed 3 September 2013).

43. Panel on Dietary Antioxidants and Related Compounds, Subcommittees on Upper Reference Levels of Nutrients and Interpretation and Uses of DRIs, Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. Dietary reference intakes for vitamin C, vitamin E, selenium and carotenoids. Washington, DC: National Academy Press; 2000 (http://www.nap.edu/openbook.php?record_id=9810&page=R, accessed 3 September 2013).

44. Institute of Medicine. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc Washington, DC: National Academy Press; 2002 (http://www.nap.edu/openbook.php?isbn=0309072794, accessed 3 September 2013).

45. Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database Syst. Rev. 2012;(11):CD004905. doi: 10.1002/14651858.CD004905.pub3.

46. Haider B, Yakoob M, Bhutta Z. Effect of multiple micronutrient supplementation during pregnancy on maternal and birth outcomes. BMC Public Health, 2011;11(Suppl. 3):S19. doi: 10.1186/1471-2458-11-S3-S19.

47. Allen LH, Peerson JM, Olney DK. Provision of multiple rather than two

or fewer micronutrients more effectively improves growth and other outcomes in micronutrient-deficient children and adults. J. Nutr. 2009;139(5):1022–30.

48. Irlam JH, Visser MME, Rollins NN, Siegfried N. Micronutrient supplementation in children and adults with HIV infection. Cochrane Database Syst. Rev. 2010;(12):CD003650. doi: 10.1002/14651858.CD003650.pub3.

49. Siegfried N, Irlam JH, Visser ME, Rollins NN. Micronutrient supplementation in pregnant women with HIV infection. Cochrane Database Syst. Rev. 2012;(3):CD009755. doi: 10.1002/14651858.CD009755.

50. Human energy requirements. Report of a Joint FAO/WHO/UNU Expert Consultation. Rome, 17–24 October 2001. FAO food and nutrition technical report series. Rome: Food and Agriculture Organization of the United Nations; 2004 (ftp://ftp.fao.org/DOCREP/FAO/007/y5686e/y5686e00.pdf, accessed 3 September 2013).

51. Protein and amino acid requirements in human nutrition. Report of a Joint WHO/FAO/UNU Expert Consultation. Geneva: World Health Organization; 2007 (http://whqlibdoc.who.int/trs/who_trs_935_eng.pdf, accessed 3 September 2013).

52. Rasmussen KM, Yaktine AL, editors. Weight gain during pregnancy. Reexamining the guidelines. Washington, DC: National Academies Press; 2009 (http://www.nap.edu/openbook.php?record_id=12584, accessed 3 September 2013).

53. Singh M, Mynak ML, Kumar L, Mathew JL, Jindal SK. Prevalence and risk factors for transmission of infection among children in household contact with adults having pulmonary tuberculosis. Arch. Dis. Child. 2005;90:624–8.

54. Moran-Mendoza O, Marion SA, Elwood K, Patrick D, FitzGerald JM. Risk factors for developing tuberculosis: a 12-year follow-up of contacts of tuberculosis cases. Int. J. Tuberc. Lung Dis. 2010;14(9):1112–9.

55. Topley JM, Maher D, Mbewe LN. Transmission of tuberculosis to contacts of sputum positive adults in Malawi. Arch. Dis. Child. 1996; 74(2):140–3.

56. Downes J. An experiment in the control of tuberculosis among Negroes. Milbank Mem. Fund Q. 1950;28(2):127–59.

57. Expert advisory panels and committees. Geneva: World Health

Organization; 2010 (http://www.who.int/rpc/ expert_panels/Factsheet_EAP2010.pdf, accessed 3 September 2013).

58. United Nations System Standing Committee on Nutrition (http://www.unscn.org/, accessed 3 September 2013).

59. World Health Organization. Nutrition (http://www.who.int/nutrition/en/, accessed 3 September 2013).

60. Scoping meeting for the development of guidelines on nutritional/food support to prevent TB and improve health status among TB patients. Meeting report, Geneva, 2–4 November 2009. Geneva: World Health Organization; 2010 (http://www.who.int/nutrition/publications/nutandtb_meeting_report/en/index.html, accessed 3 September 2013).

61. The Cochrane Collaboration. Cochrane handbook for systematic reviews of interventions. Version 5.1.0. York: The Cochrane Collaboration; 2011 (http://www.cochrane.org/training/cochrane-handbook, accessed 3 September 2013).

62. Papathakis P. Supplementary information. Population level nutritional interventions which could reduce the progression from latent to active TB. 2011.

63. Papathakis P. Supplementary information. Energy requirements in patients with tuberculosis and other pulmonary diseases. 2011.

64. GRADE Working Group (http://www.gradeworkinggroup.org/ , accessed 3 September 2013).

65. Guyatt G et al. GRADE guidelines 1. Introduction – GRADE evidence profiles and summary of findings tables. J. Clin. Epidemiol. 2011;64:383–94 (http://dx.doi.org/10.1016/j.jclinepi.2010.04.026, accessed 3 September 2013).

66. Basic documents, 47th ed. Geneva: World Health Organization; 2009 (http://apps.who.int/gb/bd/, accessed 3 September 2013).

67. Guidelines for declaration of interests (WHO experts). Geneva: World Health Organization; 2010.

68. WHO, The STOP TB Strategy. Building on and enhancing DOTS to meet TB-related Millennium Development Goals. Geneva: World Health Organization; 2006 (http://www.who.int/tb/publications/2006/stop_tb_strategy.pdf, accessed 3 September 2013).

69. Tuberculosis Coalition for Technical Assistance. International Standards for Tuberculosis Care (ISTC). The Hague: Tuberculosis Coalition for Technical Assistance; 2006

(http://www.who.int/tb/publications/2006/istc_report.pdf, accessed 3 September 2013).

70. Ralph AP, Kelly PM, Anstey NM. L-arginine and vitamin D: novel adjunctive immunotherapies in tuberculosis. Trends Microbiol. 2008;16(7):336–44. doi: 10.1016/j.tim.2008.04.003.

71. Classification of malnutrition in adults: body mass index, In: Management of severe malnutrition: a manual for physicians and other health workers. Geneva: World Health Organization; 1999:37–38.

72. WHO. Growth reference data for 5–19 years (http://www.who.int/growthref/en/, accessed 3 September 2013).

73. World Health Organization, United Nations Children's Fund. WHO child growth standards and the identification of severe acute malnutrition in infants and children. A joint statement by the World Health Organization and the United Nations Children's Fund. Geneva: World Health Organization and United Nations Children's Fund; 2009 (http://www.who.int/nutrition/publications/severemalnutrition/9789241598163_eng.pdf, accessed 3 September 2013).

74. World Health Organization. The WHO child growth standards (http://www.who.int/childgrowth/en/, accessed 3 September 2013).

75. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. Geneva: World Health Organization; 1995 (WHO Technical Report Series 854) (http://www.who.int/childgrowth/publications/physical_status/en/, accessed 3 September 2013).

76. Cegielski JP, McMurray DN. Tuberculosis: nutritional management. In: Allen LH, Prentice A, editors. Encyclopedia of human nutrition, 3rd ed. Oxford: Academic Press, Elsevier Ltd; 2013:293–8.

77. World Health Organization, Food and Agriculture Organization of the United Nations. Nutritional care and support for people living with HIV/AIDS: a training course. Geneva: World Health Organization; 2009 (http://www.who.int/nutrition/publications/hivaids/9789241591898/en/index.html, accessed 3 September 2013).

78. The International Union Against Tuberculosis and Lung Disease, World Health Organization. Collaborative framework for care and control of tuberculosis and diabetes.

Geneva: World Health Organization; 2011 (http://whqlibdoc.who.int/publications/2011/9789241502252_eng.pdf, accessed 3 September 2013).

79. World Health Organization. Tuberculosis (http://www.who.int/tb/about/en/index.html, accessed 3 September 2013).

80. World Health Organization. e-Library of Evidence for Nutrition Actions (eLENA) (http://www.who.int/elena/en, accessed 3 September 2013).

81. Evidence-Informed Policy Network (EVIPNet) (http://global.evipnet.org, accessed 3 September 2013).

82. Jahnavi G, Sudha CH. Randomised controlled trial of food supplements in patients with newly diagnosed tuberculosis and wasting. Singapore Med. J. 2010;51(12):957–62.

83. 83. Martins N, Morris P, Kelly PM. Food incentives to improve completion of tuberculosis treatment: randomised controlled trial in Dili, Timor-Leste. BMJ, 2009;339:b4248. doi: 10.1136/bmj.b4248.

84. Paton NI, Chua YK, Earnest A, Chee CB. Randomized controlled trial of nutritional supplementation in patients with newly diagnosed tuberculosis and wasting. Am. J. Clin. Nutr. 2004;80:460–5.

85. PrayGod G et al. The effect of energy-protein supplementation on weight, body composition and handgrip strength among pulmonary tuberculosis HIV-co-infected patients: randomised controlled trial in Mwanza, Tanzania. Br. J. Nutr. 2012;107(2):263–71. doi: 10.1017/S0007114511002832.

86. Sudarsanam TD et al. Pilot randomized trial of nutritional supplementation in patients with tuberculosis and HIV-tuberculosis coinfection receiving directly observed short-course chemotherapy for tuberculosis. Trop. Med. Int. Health, 2011;16(6):699–706. doi: 10.1111/j.1365–3156.2011.02761.x.

87. Loto OM, Awowole I. Tuberculosis in pregnancy: a review. J. Pregnancy, 2012;2012:379271. doi:10.1155/2012/379271.

88. Mehta S et al. A randomized trial of multivitamin supplementation in children with tuberculosis in Tanzania. Nutr. J. 2011;10:120. doi:10.1186/1475-2891-10-120.

89. PrayGod G. et al. Daily multi-micronutrient supplementation during tuberculosis treatment increases weight and grip strength among HIV-uninfected but not HIV-infected patients in Mwanza, Tanzania. J. Nutr. 2011;141:685–91. doi: 10.3945/jn.110.131672.

90. Range N, Andersen AB, Magnussen P, Mugomela A, Friis H. The effect of micronutrient supplementation on treatment outcome in patients with pulmonary tuberculosis: a randomized controlled trial in Mwanza, Tanzania. Trop. Med. Int. Health, 2005;10(9):826–32.

91. Semba RD et al. Micronutrient supplements and mortality of HIV-infected adults with pulmonary TB: a controlled clinical trial. Int. J. Tuberc. Lung Dis. 2007;11(8):854–9.

92. Villamor E et al. A trial of the effect of micronutrient supplementation on treatment outcome, T cell counts, morbidity, and mortality in adults with pulmonary tuberculosis. J. Infect. Dis. 2008;197(11):1499–505. doi: 10.1086/587846.