
The effectiveness of interventions to manage moderate and severe acute child malnutrition in low- and middle-income countries: a systematic review

Jai K. Das, Hasana Bilal, Rehana A. Salam, Zulfiqar A. Bhutta

Submitted to the Coordinating Group of:

- | | |
|-------------------------------------|--|
| <input type="checkbox"/> | Crime and Justice |
| <input type="checkbox"/> | Education |
| <input type="checkbox"/> | Disability |
| <input checked="" type="checkbox"/> | International Development |
| <input checked="" type="checkbox"/> | Nutrition |
| <input type="checkbox"/> | Social Welfare |
| <input type="checkbox"/> | Methods |
| <input type="checkbox"/> | Knowledge Translation and Implementation |
| <input type="checkbox"/> | Other: |

Plans to co-register:

- | | | | | | |
|-------------------------------------|-------|--------------------------|----------|--------------------------|-------|
| <input type="checkbox"/> | No | | | | |
| <input type="checkbox"/> | Yes | <input type="checkbox"/> | Cochrane | <input type="checkbox"/> | Other |
| <input checked="" type="checkbox"/> | Maybe | | | | |

Date submitted:

Date revision submitted:

Approval date:

Title of the review

The effectiveness of interventions to prevent and manage acute child malnutrition in low- and middle-income countries: a systematic review

Background

Globally, 155 million children under five years old are stunted (low height-for-age), and 52 million are wasted (low weight-for-height) due to inadequate dietary intake and or repeated infections (Hayashi, 2017). These burdens are especially high in low- and middle- income countries. Malnutrition also leads to 3.1 million global child deaths annually (Black, 2013). Infants and children are the most vulnerable groups, particularly during the first two years of life when nutritional needs are higher for growth and development (Victora, 2008). Undernutrition during this period can have long-lasting, and potentially irreversible, consequences for child health and well-being (Martins, 2011).

Acute malnutrition is classified as mild, moderate or severe based on anthropometric measurements (WHO, 2000). The World Health Organization provides global guidelines for the management of acute malnutrition towards standardizing treatment practices across countries (WHO, 1999). These guidelines have been updated to include guidance for identification and management of malnourished infants under 6 months, fluid management in cases of severe dehydration, vitamin A supplementation, use of antibiotics in uncomplicated severe acute malnutrition (SAM), therapeutic feeding approaches, community-based management of acute malnutrition, and management of HIV-infected children with severe acute malnutrition (WHO, 2013; Trehan, 2013).

Evidence suggests with effective inpatient treatment, mortality from SAM can be reduced to < 5%. (Ashworth, 2003). In addition, studies have shown that community-based care of SAM using ready-to-use therapeutic foods (RUTF) or home-based therapy with locally-prepared therapeutic diets can result in recovery rates that are higher than > 90% (Manary, 2004).

However, barriers and challenges in implementation of global guidelines exist at the country level. There is a need for rigorous review of implementation experiences using facility- and community-based programme strategies to generate evidence for effective delivery approaches for the management of acute malnutrition. Also, the effectiveness of using antibiotics prophylactically in uncomplicated SAM cases requires further study (Alcoba, 2013). As existing reviews (see below for the list of existing reviews) only focus on a specific population or intervention, gaps in knowledge require a broader review of available evidence. Therefore, we aim to systematically review and assess current evidence on the effectiveness of

interventions as well as programmes and/or guidelines that have been adapted to manage children with acute malnutrition.

Objectives

1. What is the effectiveness of community-based strategies to prevent and manage moderate and severe acute malnutrition?
2. What is the effectiveness of facility-based strategies to prevent and manage moderate and severe acute malnutrition?
3. What is the effectiveness of prophylactic use of antibiotics to manage uncomplicated severe acute malnutrition?

Existing reviews

Objectives 1-3: Supplementary feeding, community-based and facility-based strategies

Kristjansson E, Francis DK, Liberato S, Benkhalti Jandu M, Welch V, Batal M, Greenhalgh T, Rader T, Noonan E, Shea B, Janzen L, Wells GA, Petticrew M. Food supplementation for improving the physical and psychosocial health of socio-economically disadvantaged children aged three months to five years. *Cochrane Database Syst Rev* 2015, Issue 3. Art. No: CD009924. doi:10.1002/14651858.CD009924.pub2.

Visser J, McLachlan MH, Fergusson P, Volmink J, Garner P. Supplementary feeding for food insecure, vulnerable and malnourished populations - an overview of systematic reviews. *Cochrane Database Syst Rev* 2013, Issue 6. Art. No: CD010578. doi:10.1002/14651858.CD010578.

Lazzerini M, Rubert L, Pani P. Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries. *Cochrane Database Syst Rev* 2013, Issue 6. Art. No: CD009584. doi:10.1002/14651858.CD009584.pub2.

Lenters LM, Wazny K, Webb P, Ahmed T, Bhutta ZA. Treatment of severe and moderate acute malnutrition in low- and middle-income settings: a systematic review, meta-analysis and Delphi process. *BMC Public Health* 2013;13(3):S23. doi:10.1186/1471-2458-13-S3-S23.

Schoonees A, Lombard M, Musekiwa A, Nel E, Volmink J. Ready-to-use therapeutic food for home-based treatment of severe acute malnutrition in children from 6 months to 5 years of age. *Cochrane Database Syst Rev* 2013, Issue 6. Art. No: CD009000. doi:10.1002/14651858.CD009000.pub2.

Picot, J., Hartwell, D., Harris, P., Mendes, D., Clegg, A. J., & Takeda, A. The effectiveness of interventions to treat severe acute malnutrition in young children: a systematic review. *Health Technol Assess* 2012; 16(19):1-316. doi: 10.3310/hta16190.

Gera, T. Efficacy and safety of therapeutic nutrition products for home based therapeutic nutrition for severe acute malnutrition: a systematic review. *Indian Pediatr* 2010; 47(8); 709-18.

Objective 4: Antibiotic use

Alcoba G, Kerac M, Breyse S, Salpeteur C, Galetto-Lacour A, Briend A, Gervaix A. Do children with uncomplicated severe acute malnutrition need antibiotics? A systematic review and meta-analysis. *PLoS One* 2013;8(1):e53184. doi:10.1371/journal.pone.0053184.

Lazzerini M, Tickell D. Antibiotics in severely malnourished children: systematic review of efficacy, safety and pharmacokinetics. *Bull World Health Organ* 2011;89:594-607. doi:10.2471/BLT.10.084715.

Intervention

The following interventions targeting children under 5 years of age having moderate or severe acute malnutrition in low- and middle-income countries will be included:

- Community-based prevention and management
- Facility-based prevention and management
- Antibiotic use for severe acute malnutrition
- Micronutrients and Vitamin A supplementation
- or a combination of the above-mentioned interventions

These interventions will be compared against no intervention, standard of care (whatever is applicable in the setting the study was conducted), or placebo (in the case of drug interventions). We will also compare inpatient treatment to ambulatory treatment for children with moderate and severe acute malnutrition.

Population

The target population is children under 5 years of age having moderate or severe acute malnutrition in low- and middle-income countries.

Outcomes

Primary outcomes

- Recovery rate
- Weight gain
- Wasting
- Mid-upper arm circumference
- Mortality

Secondary outcomes

- Stunting
- Underweight
- Deterioration or relapse

Study designs

We will systematically search, select, appraise the quality of, and synthesize the relevant literature. We will search for relevant primary studies with the following designs:

- Randomized controlled trials (RCTs) including parallel and crossover trials
- Controlled before-after studies
- Interrupted time series designs (with 3 time points before and after the intervention)
- Observational studies with a control group
- Large-scale program evaluations including a control group

Pre-post studies without a control group will not be included.

References

Alcoba, G., Kerac, M., Breyse, S., Salpeteur, C., Galetto-Lacour, A., Briend, A., & Gervais, A. (2013). Do children with uncomplicated severe acute malnutrition need antibiotics? A systematic review and meta-analysis. *PLoS One*, 8(1), e53184. <https://doi.org/10.1371/journal.pone.0053184>.

Ashworth, A. (2003). *Guidelines for the inpatient treatment of severely malnourished children*. [Geneva]: World Health Organization.

Black, R.E., Victora, C.G., Walker, S.P., Bhutta, Z.A., Christian, P., de Onis, ... Maternal and Child Nutrition Study Group. (2013). Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet*, 382(9890), 427-451. [http://dx.doi.org/10.1016/S0140-6736\(13\)60937-X](http://dx.doi.org/10.1016/S0140-6736(13)60937-X).

Hayashi, C., Krusevec, J., Kumapley, R., Mehra, V., de Onis, M., Borghi, E., ... Serajuddin, U. (2017). *Levels and trends in child malnutrition. UNICEF/WHO/World Bank Group joint child malnutrition estimates: Key findings of the 2017 edition*. [New York]: UNICEF. http://www.who.int/nutgrowthdb/jme_brochure2017.pdf.

Manary, M. J., Ndkeha, M., Ashorn, P., Maleta, K., Briend, A. (2004). Home based therapy for severe malnutrition with ready-to-use food. *Archives of Disease in Childhood*, 89(6), 557-561. doi: 10.1136/adc.2003.034306.

Martins, V. J. B., Toledo Florêncio, T. M. M., Grillo, L. P., Franco, M. do C. P., Martins, P. A., Clemente, A. P. G., ... Sawaya, A. L. (2011). Long-Lasting Effects of Undernutrition. *International Journal of Environmental Research and Public Health*, 8(6), 1817–1846. <http://doi.org/10.3390/ijerph8061817>.

Trehan, I., Goldbach, H. S., LaGrone, L. N., Meuli, G. J., Wang, R. J., Maleta, K. M., & Manary, M.

J. (2013). Antibiotics as part of the management of severe acute malnutrition. *New England*

Journal of Medicine, 368(5), 425-435. doi: 10.1056/NEJMoa1202851.

Victora, C. G., Adair, L., Fall, C., Hallal, P. C., Martorell, R., Richter, L., & Sachdev, H. S. (2008).

Maternal and child undernutrition: consequences for adult health and human capital. *Lancet*,

371(9609), 340-357. doi: 10.1016/s0140-6736(07)61692-4.

WHO. (2013). *Guideline: Updates on the management of severe acute malnutrition in infants and*

children. [Geneva]: World Health Organization. http://apps.who.int/iris/bitstream/10665/95584/1/9789241506328_eng.pdf.

WHO. (2000). *Management of the child with a serious infection or severe malnutrition: Guidelines for*

care at the first-referral level in developing countries. [Geneva]: World Health Organization.

http://apps.who.int/iris/bitstream/10665/42335/1/WHO_FCH_CAH_00.1.pdf.

WHO. (1999). *Management of severe malnutrition: A manual for physicians and other senior health workers*.

[Geneva]: World Health Organization.

<http://apps.who.int/iris/bitstream/10665/41999/1/a57361.pdf>.

Review authors

Lead review author: The lead author is the person who develops and co-ordinates the review team, discusses and assigns roles for individual members of the review team, liaises with the editorial base and takes responsibility for the on-going updates of the review.

Name: Jai K. Das

Title: Assistant Professor

Affiliation: Division of Women and Child Health, Aga Khan University

Address: Stadium Road

City, State, Province or County: Karachi, Sindh

Post code: 74800

Country: Pakistan

Phone: +92.213.486.4717

Email: jai.das@aku.edu

Co-authors:

Name: Hasana Bilal

Title: Research Associate

Affiliation: Division of Women and Child Health, Aga Khan University

Address: Stadium Road

City, State, Province or County: Karachi, Sindh

Post code: 74800

Country: Pakistan

Phone: +92.213.486.4378

Email: hasana.bilal@aku.edu

Name: Rehana A. Salam

Title: Senior Lecturer

Affiliation: Division of Women and Child Health, Aga Khan University

Address: Stadium Road

City, State, Province or County: Karachi, Sindh

Post code: 74800

Country: Pakistan

Phone: +92.213.486.4717

Email: rehana.salam@aku.edu

Name: Marwah Saeed

Title: Student

Affiliation: Aga Khan University

Address: Stadium Road

City, State, Province or County: Karachi, Sindh

Post code: 74800

Country: Pakistan

Phone: +92.213.486.4378

Email: marwah.m508273@student.aku.edu

Name: Zulfiqar A. Bhutta

Title: Co-Director, Centre for Global Child Health

Affiliation: The Hospital for Sick Children

Address: 686 Bay St, 11th Floor

City, State, Province or County: Toronto, Ontario

Post code: M5G 0A4

Country: Canada

Phone: +1.416.813.7654

Email: zulfiqar.bhutta@sickkids.ca

Roles and responsibilities

- Content: Zulfiqar A. Bhutta, Jai K. Das
- Systematic review methods: Rehana A. Salam, Jai K. Das
- Statistical analysis: Rehana A. Salam, Hasana Bilal, Jai K. Das
- Information retrieval: Rehana A. Salam, Hasana Bilal, Jai K. Das, Marwah Saeed

Funding

Funding for this review came from a grant from the Bill & Melinda Gates Foundation to the Centre for Global Child Health at the Hospital for Sick Children (Grant No. OPP1137750).

Potential conflicts of interest

The authors are not aware of any conflicts of interest arising from financial or researcher interests.

Preliminary timeframe

- Date you plan to submit a draft protocol: 15 March 2018
- Date you plan to submit a draft review: 15 August 2018