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### SPECIAL ARTICLE

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# Screening and management options for severe thinness during pregnancy in India

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### Abstract

This paper answers research questions on screening and management of severe thinness in pregnancy, approaches that may potentially work in India, and what more is needed for implementing these approaches at scale. A desk review of studies in the last decade in South Asian countries was carried out collating evidence on six sets of strategies like balanced energy supplementation (BEP) alone and in combination with other interventions like nutrition education. Policies and guidelines from South Asian countries were reviewed to understand the approaches being used. A 10-point grid covering public health dimensions covered by World Health Organization and others was created for discussion with policymakers and implementers, and review of government documents sourced from Ministry of Health and Family Welfare. Eighteen studies were shortlisted covering Bangladesh, India, Nepal, and Pakistan. BEP for longer duration, preconception initiation of supplementation, and better presupplementation body mass index (BMI) positively influenced birthweight. Multiple micronutrient supplementation was more effective in improving gestational weight gain among women with better pre-supplementation BMI. Behavior change communication and nutrition education showed positive outcomes on dietary practices like higher dietary diversity. Among South Asian countries, Sri Lanka and Nepal are the only two countries to have management of maternal thinness in their country guidelines. India has at least nine variations of supplementary foods and three variations of full meals for pregnant women, which can be modified to meet additional nutritional needs of those severely thin. Under the National Nutrition Mission, almost all of the globally recommended maternal nutrition interventions are covered, but the challenge of reaching, identifying, and managing cases of maternal severe thinness persists. This

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#### KEYWORDS

(X)

India, management of maternal severe thinness, policy, pregnancy, screening for maternal severe thinness, severe thinness

### 1 | INTRODUCTION

In most low- and middle-income countries (LMICs), severe thinness– defined by the World Health Organization (WHO) as body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) below  $16^{1}$ —among women of reproductive age (15–49 years) continues to persist in selected regions, along with an increasing prevalence of overweight and obesity. Prevalence of severe thinness was estimated at 1.8% among women aged 20– 49 years across 60 LMICs.<sup>2</sup> In India, prevalence of thinness or severe thinness ranges between 2%–41%.<sup>3–12</sup> Mortality risk was twice as high among those with very low BMI (<15) compared with very high BMI (>35).<sup>13</sup> Thinness, either mild (BMI 18.49–16) or severe (BMI <16) in pregnant women increases the risk of preterm birth, small for gestational age (SGA) neonates, low birthweight (LBW; defined as <2500 g), and infant mortality.<sup>14–17</sup>

Daily requirements for all nutrients increase in pregnancy. Among pregnant women with normal pre-pregnancy weight, energy requirements increase by 350 kcal/day and protein by 7.6 g/ day in the second trimester, and 17.6 g/day in the third trimester as per Estimated Average Requirements 2020.<sup>18</sup> Pregnant women with severe thinness have higher nutrient requirements to achieve adequate gestational weight gain (GWG) compared to pregnant women with optimal BMI. In 2016, WHO recommended balanced energy and protein (BEP) supplementation for pregnant women in undernourished populations to reduce the risk of stillbirths and SGA neonates, and targeted counselling of severely thin pregnant women to increase energy-protein intake along with an array of nutritional interventions.<sup>19</sup> Earlier, in 2013, WHO recommended that pregnant women with active tuberculosis and moderate undernutrition, 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.<sup>20</sup> In the absence of medical conditions, WHO recommended an outpatient food-by-prescription program for severely thin adolescents and

adults.<sup>21</sup> In India, under the Integrated Child Development Service (ICDS) scheme, pregnant women and lactating mothers are entitled to take home ration (THR) or hot cooked food providing 600 kcal energy, 18–20 g protein, and half the daily requirement for nine essential micronutrients for 300 days a year.<sup>22</sup> However, there is no special nutritional support package for pregnant women who are thin or severely thin, except those afflicted with tuberculosis.<sup>23</sup> Maternal severe thinness screening and management remains suboptimally addressed in India's public health and nutrition programs. Thus, this review provides evidence on screening and management options using a single or combination of available interventions in India and other South Asian countries, and current Indian policies, and financial and programmatic issues to screen and manage severe maternal thinness.

### 2 | MATERIALS AND METHODS

### 2.1 | Review of literature

The authors searched research articles published between January 2010 and December 2019 in two databases (Cochrane Library and PubMed). The following search string were used: "Thin OR Underweight OR Body Mass Index OR Undernutrition OR Severe underweight OR MUAC AND Pregnant OR Preconception OR Pre-pregnancy OR Adolescents AND Intervention OR Trial OR Management." After screening titles and abstracts, studies were selected from the studies extracted from the search and reference lists of original and review articles, guidelines, and reports were reviewed to obtain more relevant studies.

We used a PICO (Population, Intervention, Comparison, and Outcome of interest) format for the development of the search strategy and studies for the review were obtained based on the following inclusion criteria: original research, community-based/ population-based/facility-based study, with details on study design, sample size, study setting and interventions/strategies, and studies from only South Asian countries (Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, and Sri Lanka). Animal-based studies and any studies published in languages other than English were excluded. Studies with interventions for thinness or severe thinness (with BMI <18.5 or <16, respectively), and pregnant or under pregnancy surveillance (preconception) were included. Studies where the sample included pregnant women with both normal and low BMI and those studies with higher than 20% prevalence of thinness or with additional analysis for undernourished women were considered.

Regarding recommendations from WHO 2011, 2016, and the *Lancet* 2013,<sup>19,44-46</sup> the following interventions for effective management of maternal thinness were considered: BEP supplementation, multiple micronutrient (MMN) supplementation, nutrition education, and behavior change communication (BCC). Any combinations of these interventions were also included. Primary outcomes included LBW, SGA, preterm birth (gestation <37 weeks), GWG, improvement in maternal BMI, infant anthropometry (weight, length, and head circumference at birth), perinatal/neonatal mortality, and long-term growth. Secondary outcomes included improved compliance with supplementation, increased knowledge of dietary practices, and behavioral change (handwashing and oral hygiene).

The searched studies were reviewed by two independent researchers and discrepancies about the inclusion of studies were resolved by discussion with a third reviewer. Relevant information on study title, authors, objectives, study setting and type of population, sample size, study design, methodology, intervention(s), outcome, and results were transcribed into a predesigned data collection form.

### 2.2 | Review of guidelines

The authors accessed guidelines on or related to maternal nutrition including antenatal care (ANC) from ministerial websites of all South Asian countries and carefully scanned for interventions that may be relevant to the management of severe thinness. Country or regional nutrition programs' review reports by UNICEF, Scaling up Nutrition, and related websites were also reviewed.

### 2.3 | Development of guidelines review grid and discussions with policymakers and implementers

A guideline review grid consisting of 10 blocks was constructed covering public health dimensions covered by WHO and others, such as availability and accountability for guidelines, plans and financing, demand creation, leadership and governance, partnerships, information systems/monitoring and evaluation, capacity building, supply, institutionalized mechanisms, research, and policy dialogue. The grid was used for discussion with policymakers and implementers of proposed Indian maternal nutrition guidelines to understand the current status and gaps against each of the blocks. All available documents, such as national ANC implementation guidelines, composition tables 🛞-WILEY

of supplementary foods or therapeutic foods being given to pregnant women in India, annual plan, and record of proceedings for measuring budget outlays were collated and reviewed to understand current provisions and gaps.

Severe thinness and severe underweight have been used interchangeably in operational definitions for this article.

### 3 | RESULTS

Figure 1 presents a flowchart for the inclusion of studies in this review. Initially, 529 records were retrieved from the literature searches. Based on the title and abstract, 81 studies were selected for further screening. Based on inclusion criteria, relevance, and availability of full text, 18 studies were chosen for the review.<sup>25-43</sup>

Table 1 presents the detailed characteristics of the studies included in the review. Nine studies were from Bangladesh, five from India, and three from Nepal. There was one multi-country controlled study that included cohorts from India.<sup>32</sup> Eleven studies were randomized controlled trials (RCTs) and the remaining seven studies were case-control studies. Included studies focused on women of low socioeconomic status, with a high prevalence of thinness. Seven studies focused on only thin or severely thin pregnant women, defined as mid-upper arm circumference (MUAC) ≤22.1 cm<sup>26</sup> or BMI < 18.5.<sup>27,36,37,39-41</sup> In the remaining studies, there was a mixed sample of participants including both underweight and normal BMI. However, the prevalence of thinness was high, and only one among these reported a subgroup analysis for thin mothers.<sup>29</sup> None of the studies had subgroup analysis for severely thin pregnant women. Five studies involved women under pregnancy surveillance.<sup>25,28-30,32</sup> whereas 13 studies recruited women who were already pregnant, and intervention was started after pregnancy confirmation. All studies, except one, included newborns for studying the effect of the intervention on outcome measures such as LBW and infant anthropometry.

There were three studies with only BEP supplementation,<sup>25-27</sup> three with only MMN supplementations,<sup>28-30</sup> three studies involving both food supplementation and MMN supplementations,<sup>31-33</sup> two studies with only nutrition education,<sup>35,36</sup> five studies with nutrition education and BEP supplementation,<sup>37-41</sup> and two studies involving only BCC.<sup>43,44</sup>

### 3.1 | BEP supplementation

Three RCTs involving 6264 women evaluated the effect of BEP supplementation on neonatal, perinatal, and maternal outcomes.<sup>25-27</sup> Potdar et al.<sup>25</sup> reported a trend toward a higher birthweight for 1094 infants (+48 g; 95% Cl, 1–96 g; P = 0.046) of women in the treatment group who received a treatment snack resembling local street food containing a mix of micronutrient-dense green leafy vegetables (such as spinach, coriander), milk powder, and dry fruits from more than 90 days before pregnancy until delivery. However, no overall

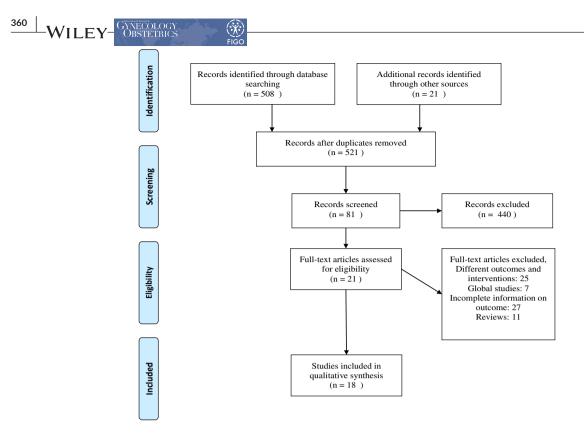


FIGURE 1 Flow chart for selection of studies for desk review

positive effect on birth weight was observed for the entire cohort (26 g; 95% Cl, -15 to 68 g; P = 0.22). The cluster RCT from Bangladesh involving 87 undernourished pregnant (defined as MUAC <22.1 cm) women treated until delivery with a locally produced BEP supplement found no significant differences in birth weight, whereas the MUAC of infants at 6 months of age was higher in the intervention group (12.83  $\pm$  0.62 vs 12.01  $\pm$  0.21 cm; P < 0.05). No significant difference was observed in other maternal and infant outcomes.<sup>26</sup> The study from Bangalore did not observe any significant difference in GWG, birthweight, birth length, or gestational age in 12 underweight pregnant women (BMI <18.5) who were provided a daily food supplement.<sup>27</sup>

### 3.2 | MMN supplementation

Three studies involving 50 693 women with MMN supplementation found a significant increase in birthweight and reduction in the prevalence of LBW babies.<sup>28-30</sup> In the RCT from rural Nepal by Christian et al.,<sup>28</sup> the intervention was spread across four arms (supplementation with only folic acid, iron-folic acid (IFA), iron, folic acid and zinc, and a mix of 11 micronutrients (vitamin D, vitamin E, vitamin B1, vitamin B2, niacin, vitamin B6, vitamin B12, vitamin C, vitamin K, copper, and magnesium) against control; all groups were supplemented with vitamin A (irrespective of control or treatment) including 4926 pregnancies and 4130 infants. The authors reported a 16% decline in LBW in the intervention group supplemented with IFA (OR 0.84; 95% CI, 0.72–0.99), and a 14% decline of the same in the MMN group (OR 0.86; 95% CI, 0.74–0.99). Although linear growth remained unaffected

in either the IFA or MMN group, head and chest circumference were significantly higher in both groups (P = 0.012 and P < 0.001, respectively). There was no significant association between any of these supplements and neonatal or perinatal mortality.<sup>28</sup>

Another RCT from Nepal reported that MMN supplementation (per UNIMMAP, a MMN tablet providing RDAs for thiamine, vitamin A, riboflavin, vitamin B6, vitamin B12, niacin, folic acid, vitamin C, iron, copper, iodine, selenium, vitamin D, vitamin E, and zinc) contributed to a 77 g increase (95% Cl, 24–130; P = 0.04) in birthweight compared with the control arm with only IFA supplementation.<sup>29</sup> Mean birthweight was also higher in women with a BMI ≥18.5 (2804 g vs 2688 g) who received the intervention. In the analysis stratified by BMI, the difference in birthweight and LBW only remained significant for mothers with BMI ≥18.5 (birthweight: +83 g, 95% Cl, 20–146; P = 0.010; reduction in LBW, OR 0.69; 95% Cl, 0.52–0.93; P = 0.014). No long-term benefits concerning child growth were noted.<sup>29</sup>

The JiVitA-3 trial from Bangladesh involving 127 282 women under pregnancy surveillance (44 567 pregnancies), with almost 40% of the sample having a BMI <18.5, found a significant reduction in preterm birth (RR 0.85; 95% CI, 0.80–0.91; P < 0.001), LBW (RR 0.88; 95% CI, 0.85–0.91; P < 0.001), and increase in recorded birth weight (54 g; 95% CI, 41–66) in the intervention group provided with a mix of 15 micronutrients (dosage similar to UNIMMAP).<sup>30</sup>

### 3.3 | Combined BEP and MMN supplementation

Three studies, including 12 900 women, reported the use of BEP supplementation as well as MMN supplementation, and one follow-up

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| Outcomes             | Birth weight:<br>No significant difference<br>(+26 g; 95% Cl, -15, 68 g;<br>P = 0.22)<br>For mothers with<br>supplementation $\geq$ 90 days,<br>higher birth weight was<br>observed in the treatment<br>group (+48 g; 95% Cl, 1,<br>96 g; $P = 0.046$ )<br>Increased effect with maternal<br>BMI (p-interaction = 0.001)<br>LBW:<br>No significant effect<br>(OR 0.83; 95% Cl: 0.66, 1.98;<br>P = 0.10)<br>Small for gestational age births:<br>Not significant (OR 0.89; 95%<br>Cl, 0.70, 1.13; $P = 0.33$ )<br>Preterm births:<br>Not significant (treatment: 13%;<br>control: 12%; $P = 0.60$ ) | Birthweight: No significant<br>difference (intervention<br>group: 2.91 $\pm$ 0.19; control<br>group: 2.72 $\pm$ 0.13; $P = 0.13$ )<br>LBW: No significant difference<br>in proportion of LBW babies<br>(event rate: 0.04 vs 0.16;<br>P = 0.28)<br>MUAC at 6 months: Significantly<br>higher in the intervention<br>group (12.83 $\pm$ 0.62 vs<br>12.01 $\pm$ 0.21; $P < 0.05$ ) |
| Type of Intervention | Food supplementation<br>Treatment snack: fresh and<br>dried GLVs, milk, dried<br>fruit<br>Energy: 1.65 kcal<br>Protein: 6.4 g<br>Micronutrients (vitamin<br>B12, folate, riboflavin,<br>iron, β-carotene,<br>calcium): 10%-23% of<br>WHO recommended<br>nutrient intake (RNI)<br>Control snack: potato,<br>tapioca, onion  | BEP supplementation:<br>pigeon pea (48 g), banana<br>(60 g), sugar (28 g),<br>peanuts (15 g), whole<br>milk powder (10 g),<br>sesame seeds (10 g),<br>iodized salt (2 g)<br>Energy: 522 kcal<br>Protein: 19.5 g<br>Control group: No food<br>supplementation  |
| Study duration       | Six days a week<br>from 90 days<br>before<br>pregnancy<br>until delivery   | Daily<br>supplements<br>from<br>enrolment<br>(Feb 2013 to<br>Feb 2015) in<br>the study to<br>delivery   |
| Respondents          | Women: 3205 in<br>the treatment<br>group (1106<br>pregnancies,<br>anthropometry<br>for 662 babies)<br>3308 in the control<br>group (1185<br>pregnancies,<br>anthropometry<br>for 698 babies)   | Thin pregnant<br>women (MUAC<br><22.1 cm)   |
| Sample size          | 6153   | 8   |
| Location             | tation<br>India (Mumbai)   | Bangladesh<br>(Pirganj,<br>Rangpur)   |
| Design               | BEP) supplemer<br>RCT  | RCT   |
| Study objective      | Intervention: Balanced energy protein (BEP) supplementation<br>Potdar et al. To study the effect RCT In<br>2014 <sup>25</sup> of improving<br>the quality and<br>quantity of<br>micronutrient<br>intake in<br>women on the<br>birthweight of<br>infants  | To study the efficacy<br>of locally<br>produced BEP<br>supplementation<br>during pregnancy<br>to improve birth<br>outcomes  |
| Reference            | Intervention: E<br>Potdar et al.<br>2014 <sup>25</sup>   | Stevens<br>et al.<br>2018 <sup>26</sup>   |

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TABLE 1 Characteristics of the studies included in the review of available interventions for managing severe maternal thinness in South Asia

(Continues)

|             |                      | FIGO  |  |                                       |
|-------------|----------------------|---|--|---------------------------------------|
|             | Outcomes             | Maternal weight gain: Not<br>significant<br>Birth weight, length, gestational<br>age at birth: Not significant  | LBW: with control group<br>Arm 2: IFA intervention<br>Reduced prevalence (34% from<br>43%), RR <sub>Arm2</sub> : 0.84 (95% Cl,<br>0.72, 0.99)<br>Arm 4: MMN intervention<br>Reduction in LBW babies by<br>14%<br>RR <sub>Am4</sub> : 0.86 (95% Cl, 0.74, 0.99)<br>Small for gestational age:<br>Not significant (P = 0.1712)<br>Dreterm hirth: | No significant reduction $(P = 0.77)$ |
|             | Type of Intervention | Micronutrient<br>supplementation:<br>First trimester: 5 mg folic<br>acid/days<br>Second and third trimester:<br>0.5 mg folic acid/d, iron<br>(45 mg), calcium (1 g/<br>day) along with two<br>doses of tetanus toxoid<br>Food supplementation:<br>Daily dietary supplement of<br>energy and protein<br>Food supplementation: 3<br>Ladoos/day<br>Crushed roasted peanuts,<br>puffed rice, skimmed<br>mik, clarified butter,<br>unrefined sugar<br>Energy: 300 kcal/days<br>Protein: 15 g protein/day<br>Control group: No food<br>supplement | Micronutrient<br>supplementation:<br>Control group: No<br>supplementation<br>Arm 1: Folic acid<br>Arm 2: Folic acid and iron<br>Arm 3: Folic acid, iron, zinc<br>Arm 4: Multiple<br>micronutrients   |                                       |
|             | Study duration       | 12 ± 1 weeks of gestation to delivery   | From 80 days<br>until<br>12 weeks<br>after delivery  |                                       |
|             | Respondents          | Pregnant women<br>with BMI <18.5<br>and at <13 weeks<br>of gestation  | Women under<br>pregnancy<br>surveillance;<br>2007 pregnancies<br>Mean BMI: 19.9<br>Mean weight: 43.5 kg  |                                       |
|             | Sample size          | 24  | 4926<br>pregnant<br>women<br>and 4130<br>infants   |                                       |
|             | Location             | India<br>(Bangalore)  | Nepal (Sarlahi)  |                                       |
|             | Design               | Case-control India<br>(B  | RCT  |                                       |
| (Continued) | Study objective      | To determine the<br>effect of dietary<br>supplementation<br>with protein<br>and energy<br>on pregnancy<br>outcomes  | Christian To assess the effect RCT<br>et al. of antenatal<br>2003 <sup>28</sup> multiple<br>micronutrient<br>supplementation<br>on birth outcomes  |                                       |
| TABLE 1 (C  | Reference            | Dwarkanath<br>et al.<br>2016 <sup>27</sup>  | Christian<br>et al.<br>2003 <sup>28</sup>  |                                       |

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| TABLE   |

| Outcomes             | All respondents:<br>Birthweight:<br>+77 g (95% Cl, 24–130 g);<br>P = 0.04<br>Results for perinatal mortality,<br>neonatal mortality,<br>and stillbirths were not<br>significant<br>No significant differences<br>were also reported for<br>infant length and head<br>circumference<br>Subgroup (BMI <18.5):<br>No significant difference for<br>birthweight ( $P = 0.274$ ) | Birthweight:<br>Increase in birthweight: $+54$ g<br>( $95\%$ Cl, $41-66$ g)<br>LBW RR: 0.88 ( $95\%$ Cl, 0.85,<br>0.91; $P < 0.001$ )<br>Preterm birth:<br>Reduced risk, RR: 0.85 ( $95\%$ Cl,<br>0.80, 0.91; $P < 0.001$ )<br>Small for gestational age:<br>Not significant, RR: 0.98 ( $95\%$<br>Cl, 0.98, 1.20)<br>Not significant, RR: 0.98 ( $95\%$<br>Cl, 0.88, 1.20) |
|----------------------|---|---|
| Type of Intervention | Multiple micronutrient<br>supplementation:<br>Intervention group: As<br>per UNIMMAP; for<br>Hb <70 g/L, extra<br>iron 60 mg daily, along<br>with antihelminthic<br>treatment; for night-<br>blindness, VitA 2000 ug<br>Control group: Iron (60 mg),<br>folic acid (400 ug)  | Multiple micronutrient<br>supplementation:<br>Intervention group: VitA,<br>thiamine, VitB <sub>a</sub> , VitB <sub>a</sub> ,<br>VitC, VitD, VitE, copper,<br>iodine, selenium, zinc<br>Control group: Iron, folic<br>acid   |
| Study duration       | From 112 days<br>until delivery<br>(Aug 11,<br>2002-July<br>2004)   | Median<br>enrolment at<br>9 weeks until<br>12 weeks<br>after delivery   |
| Respondents          | Women under<br>pregnancy<br>surveillance:<br>600 control (568<br>deliveries), 600<br>intervention (571<br>deliveries)<br>Subgroup: Stratified<br>by BMI (BMI<br><18.5)  | Women under<br>pregnancy<br>surveillance:<br>44 567<br>pregnancies<br>recruited;<br>39.9% women with<br>BMI <18.5   |
| Sample size          | 1200  | 127 282   |
| Location             | Nepal<br>(Janakpur)   | Bangladesh  |
| Design               | RCT   | RCT   |
| Study objective      | To assess the effect<br>of antenatal<br>multiple<br>micronutrient<br>supplementation<br>on birth outcomes   | To study the effect<br>of antenatal MM<br>supplementation<br>vs IFA<br>supplementation<br>on birth outcomes   |
| Reference            | Osrin et al.<br>2005 <sup>29</sup>  | West et al.<br>2014 <sup>30</sup>   |
|                      |   |   |

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> Significant difference was also reported for arm, head, and chest circumference.

| TABLE 1 (0   | (Continued)   |                         |   |             |   |  |   |   |
|--|---|-------------------------|---|-------------|---|--|---|---|
| Reference  | Study objective   | Design                  | Location  | Sample size | Respondents   | Study duration   | Type of Intervention  | Outcomes  |
| Intervention:<br>Matias et al.<br>2016 <sup>31</sup> | Intervention: BEP and multiple micronutrient supplementation<br>Matias et al. To assess the RCT Ba<br>2016 <sup>31</sup> efficacy of lipid-<br>based nutrient<br>supplements on<br>maternal weight<br>gain and MUAC | rient supplemeni<br>RCT | tation<br>Bangladesh<br>(Rangpur<br>and<br>Dinajpur)            | 4011        | Pregnant women<br>recruited at<br><20 weeks'<br>gestation<br>Subgroup 1: Women<br>aged >25 years<br>Subgroup 2: Women<br>in the lowest<br>quartile for height   | All respondents:<br>Group 1:<br>pregnancy<br>and 6 months<br>postpartum<br>Group 2: Daily<br>during<br>pregnancy<br>and every<br>alternate day<br>for 3 months<br>after delivery | Food supplementation:<br>Lipid-based nutrient<br>supplementation (LNSs)<br>and micronutrient<br>supplementation,<br>randomized into two<br>groups:<br>Group 1: Women received<br>LNS-PL (20 g/day)<br>Energy: 118 kcal<br>Group 2: Women received<br>1 tab (60 mg Fe and<br>400 mg FA)  | All respondents:<br>Maternal weight gain per week:<br>Not significant across<br>intervention groups<br>( $P = 0.56$ )<br>Change in MUAC:<br>Not significant across<br>intervention groups<br>( $P = 0.27$ )<br>Respondent subgroup 1:<br>Multiparous women in the<br>LNS-PL group had higher<br>weight gain by 34 g/week<br>( $P = 0.001$ )<br>Women in the LNS-PL group<br>had higher MUAC by 0.4 cm<br>( $P = 0.003$ )<br>Respondent subgroup 2:<br>Women in the LNS-PL group   |
| Hambidge<br>et al.<br>2019 <sup>32</sup>             | To study the effect<br>on newborn size<br>due to antenatal<br>micronutrient<br>supplementation  | RCT                     | DRC,<br>Guatemala,<br>North<br>Karnataka,<br>India,<br>Pakistan | 7387        | Nonpregnant<br>women; 2451<br>births with<br>nongestational<br>age-adjusted<br>(NGAA) primary<br>outcomes, 1465<br>births with GAA<br>outcomes<br>Subgroup:<br>Women with BMI<br><20; and/or<br>women with<br>GWG <lom<br>guidelines</lom<br> | 6-12 months  | Micronutrient<br>supplementation:<br>Lipid-based micronutrient<br>supplement (primary)<br>Protein-energy supplement<br>(secondary): 300 kcal<br>and 11 g of protein<br>Arm 1: Supplement from<br>≥3 months before<br>conception to delivery<br>Arm 2: Supplement from<br>second and third<br>trimesters until delivery<br>Arm 3: Control group<br>Secondary supplement was<br>only provided to the<br>subgroup of women | had greater MUAC<br>( $P = 0.004$ at 10th<br>percentile, $P = 0.014$ at 25th<br>percentile)<br>Length for age 2-scores:<br>Not significant for the overall<br>cohort<br>Positive effect size in India<br>(+0.17, $P = 0.1244$ )<br>LBW:<br>RAmm1 and Arm 3: 0.86 (95% Cl,<br>0.75, 0.98, $P = 0.0263$ )<br>RRAmm2 and Arm 3: 0.81 (95% Cl,<br>0.75, 0.93, $P = 0.0038$ )<br>Intervention initiated<br>preconception or during first<br>trimester resulted in greater<br>mean birth size and reduced<br>rates of stunting, wasting,<br>underweight, and SGA.<br>However, maternal weight<br>gain was not optimal |

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|    | Outcomes             | Significant differences<br>observed for bir thweight,<br>SGA, neonatal mortality,<br>infant mortality, and<br>under-5 mortality<br>between the two food<br>supplementation groups<br>In the follow-up study (Khan<br>et al.) there was a reduced<br>prevalence of stunting  |                                   | Dietary intake:<br>Increase in the quantity of food<br>groups consumed ( $P < 0.001$<br>for cereals, GLVs, fruits,<br>milk, fat; $P < 0.05$ for pulses,<br>roots, and tubers)<br>Improvement in nutrient intake<br>( $P < 0.001$ for all)<br>Weight gain:<br>0.40 kg per week (not<br>significant)<br>Hb levels:<br>Increase in mean Hb levels<br>(intervention group<br>$2.65 \pm 0.97$ vs control group<br>$7.85 \pm 1.58$ , $P < 0.001$ )<br>Reduction in anemia prevalence:<br>intervention group ( $78.7\%$ )<br>compared to the control<br>group ( $96\%$ ) |       |
|    | Type of Intervention | Micronutrient<br>supplementation as per<br>UNIMMAP<br>Food supplementation:<br>Roasted rice powder<br>(80 g), roasted pulse<br>powder(40 g), molasses<br>(20 g), soybean oil (6 g)<br>Energy: 608 kcal<br>Protein: 18 g of vegetable<br>protein<br>1. Early food<br>supplementation<br>2. Usual food<br>supplementation |                                   | Nutrition education:<br>Individual counselling: 30-<br>40 min at recruitment<br>Weekly home visits<br>Group meetings<br>Counselling of husband and<br>mother-in-law   |       |
|    | Study duration       | 102 days until<br>delivery  |                                   | 10-16 weeks   |       |
|    | Respondents          | Pregnant women<br>(27.4% in the<br>early food<br>supplementation<br>group and 27.7%<br>in the usual food<br>supplementation<br>group had BMI<br><18.5)  |                                   | Pregnant women: 50<br>intervention, 50<br>control   |       |
|    | Sample size          | 1478  |                                   | 100   |       |
|    | Location             | Bangladesh<br>(MINIMat)   |                                   | India<br>(Ghaziabad<br>district,<br>Uttar<br>Pradesh)   |       |
|    | Design               | RCT   |                                   | Case-control  |       |
|    | Study objective      | To study the effect<br>of multiple<br>micronutrient<br>supplements<br>and food<br>supplementation<br>on child health  | Intervention: Nutrition education | To study the<br>nutritional<br>practices in<br>undernourished<br>pregnant women<br>and assess<br>the efficacy<br>of nutrition<br>education  |       |
|    | Reference            | Persson<br>et al.<br>2012 <sup>33</sup><br>Khan et al.<br>2011 <sup>34</sup>  | Intervention: N                   | Garg and<br>Kashyap,<br>2006 <sup>35</sup>  |       |

| Outcomes             | Weight gain: Significantly<br>higher weight gain in<br>the intervention group<br>$(8.8 \pm 2.0 \text{ kg})$ compared<br>with the control<br>group $(6.9 \pm 1.4 \text{ kg})$<br>(P < 0.0001)LBW:No<br>significant difference |   | All respondents:<br>Weight gain during pregnancy:<br>Intervention vs control:<br>$7.5 \pm 1.0, 6.3 \pm 1.9$ ,<br>P < 0.001<br>69.5% of mothers in the<br>intervention group had<br>adequate weight gain (>7 kg)<br>as opposed to 49% in the<br>control group ( $P = 0.004$ )<br>LBW:<br>Lower prevalence but not<br>significant (10.8% for<br>intervention, 11.5% for<br>control, $P=1.00$ )<br>Compliance to ferrum/folate:<br>Not significant ( $P = 0.955$ )<br>Subgroup:<br>Meight gain during pregnancy:<br>Intervention vs control:<br>R $1.1 \pm 1.4, 6.3 \pm 1.3$ ,<br>P < 0.001<br>8.1 $\pm 1.4, 6.3 \pm 1.3$ ,<br>P < 0.001<br>85.7% of mothers in<br>intervention group had<br>adequate weight gain (>7 kg)<br>as opposed to 51.9% in the<br>control group ( $P < 0.044$ )<br>LBW:<br>LeW:<br>Lower prevalence but not<br>significant (6.3% for<br>intervention, 16% for<br>control, $P = 0.632$ ) |  |
|----------------------|--|---|---|--|
| Type of Intervention | Nutrition education:<br>Based on field-tested flip<br>book, handwashing,<br>and meal preparation<br>demonstration  |   | Food supplementation:<br>Roasted rice powder (80 g),<br>molasses (20 g), roasted<br>pulse powder (40 g)<br>soyabean oil (6 g)<br>Energy: 608 kcal<br>Protein: 17.9 g  |  |
| Study duration       | 9 months   |   | 6 days a week<br>from 16th<br>week of<br>pregnancy<br>until delivery  |  |
| Respondents          | Pregnant women<br>with BMI <18.5   |   | Pregnant women:<br>Intervention<br>group (BMI<br><18.5): 195<br>Control group (BMI<br>≥18.5): 261<br>Subgroup:<br>Primigravid women   |  |
| Sample size          | 50   |   | 456   |  |
| Location             | India (Jagadia<br>block,<br>Bharuch,<br>Gujarat)   |   | Bangladesh (5<br>upzillas/<br>subdistricts)   |  |
| Design               | Case-control   | d.  | control<br>study  |  |
| Study objective      | To study the effect<br>of nutrition<br>education on<br>undernourished<br>pregnant women  | Intervention: Nutrition education and BEP | To study the efficacy<br>of pregnancy<br>interventions in<br>BINP   |  |
| Reference            | Daniel et al.<br>2016 <sup>36</sup>  | Intervention: N                           | Ortolano<br>et al.<br>2003 <sup>37</sup>  |  |

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| Outcomes             | 3% rate of decline in<br>underweight prevalence per<br>month  | Birth weight:<br>Dose-response relationship<br>for increase in birthweight:<br>1.0 g/day for each day of<br>supplementation ( $P = 0.007$ )<br>In case of women with<br>postpartum weight >42 kg,<br>observed increase in<br>birthweight: 3 g/day of<br>supplementation<br>>4 months, increase in<br>birthweight of 1.8 g/day of<br>supplementation | Mean weight gain during<br>pregnancy:<br>Not significant<br>LBW:<br>Not significant<br>Equal percentages of LBW<br>babies born to both<br>groups (21% and 22%<br>respectively with or without<br>supplementation) |
| Type of Intervention | BEP supplementation:<br>(cereal-pulse mixture<br>with jaggery and oil:<br>80% carbohydrate, 12%<br>protein, 8% fat)<br>Energy: 608 kcal<br>Protein: 179 g | BEP supplementation:<br>(80 g roasted rice powder,<br>40 g roasted pulse<br>powder, 20 g molasses,<br>12 mL soyabean<br>oil, 17.9 g vegetable<br>protein)<br>Energy: 608 kcal<br>Protein: 17.9 g  | BEP supplementation:<br>Cereal-pulse mixture<br>with jaggery and oil<br>(80% carbohydrate,<br>12% protein, 8% fat)<br>600 kcal/day<br>Energy: 608 kcal<br>Protein: 18 g   |
| Study duration       | 6 days a week<br>from third<br>month of<br>pregnancy<br>to 6 months<br>after delivery   | Daily<br>supplements<br>for 4 months  | 6 days a week<br>from 16th<br>week of<br>pregnancy<br>until delivery  |
| Respondents          | Pregnant women: 68<br>participants, 215<br>nonparticipants<br>in Bangladesh<br>National Nutrition<br>Program  | Undernourished<br>pregnant women  | Pregnant women  |
| Sample size          | 283   | 619   | 1104  |
| Location             | Bangladesh<br>(subdistirct<br>Shahrasti,<br>District<br>Chandrapur)<br>BINP   | Bangladesh  | Bangladesh<br>Mymensingh<br>(BINP)  |
| Design               | Case-control  | Case-control  | Case-control  |
| Study objective      | To assess the<br>effectiveness<br>of BINP on<br>nutritional<br>outcomes in<br>pregnant women  | To study the effect of<br>supplementation<br>birthweight,<br>stratified<br>by maternal<br>postpartum<br>weight  | To assess the<br>efficacy of BINP<br>for gestational<br>weight gain in<br>pregnant women<br>and reduction of<br>low birthweight   |
| Reference            | Khan et al.<br>2005 <sup>38</sup>   | Shaheen<br>et al.<br>2006 <sup>39</sup>   | Nahar et al.<br>2008 <sup>40</sup>  |

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|                     | Outcomes             | Birth weight:<br>Intervention group infants had<br>significantly higher birth<br>weight than the control<br>group ( $p$ <0.001)<br>No significant difference in<br>birth weight between<br>the intervention<br>groups (supplemented:<br>$2664.15 \pm 360.33$ g<br>and nonsupplemented:<br>$2664.15 \pm 360.33$ g<br>and nonsupplemented:<br>$2720.18 \pm 368.63$ g) in the<br>NNP area<br>OR for normal birthweight:<br>OR for normal birthweight:<br>0.77,701)<br>OR <sub>Arm1 vs Anm2</sub> : 3.34 (95% Cl,<br>2.17,7.01) |  | Birthweight:<br>Significantly higher only in<br>DIA 1600d internantion |
|                     | Type of Intervention | BEP supplementation:<br>Roasted rice powder (80 g),<br>molasses (20 g), roasted<br>pulse powder (40 g),<br>soyabean oil (6 g)<br>Energy: 608 kcal<br>Protein: 18 g<br>Arm 1 (Control): Non-<br>NNP area, without<br>supplementation<br>Intervention Group:<br>Arm 2: NNP Area without<br>supplementation<br>Arm 3: NNP Area with  |  | BCC:<br>Community-based  |
|                     | Study duration       | 6 days a week<br>from 16th<br>week of<br>pregnancy<br>until delivery  |  | June 2014 to<br>March 2015   |
|                     | Respondents          | Undernourished<br>pregnant women  |  | Pregnant women   |
|                     | Sample size          | 565   |  | 25 092   |
|                     | Location             | Bangladesh<br>(Kapasia<br>and Sarvar,<br>Dhaka)   |  | Nepal<br>(Dhanusha,  |
|                     | Design               | Case-<br>control<br>study<br>(NNP)  | nication (BCC)                                     | RCT<br>cluster   |
| ontinued)           | Study objective      | To evaluate the<br>efficiency of the<br>National Nutrition<br>Program in<br>Bangladesh<br>for improving<br>pregnancy and<br>birth outcomes  | Intervention: Behaviour change communication (BCC) | To study the impact<br>of participatory                                |
| TABLE 1 (Continued) | Reference            | Karim et al.<br>2011 <sup>41</sup>  | Intervention: B                                    | Saville et al.<br>2018 <sup>42</sup>                                   |
|                     |                      |   |  |  |

| Reference                                | Study objective  | Design                            | Location                                     | Sample size                              | Respondents  | Study duration                                    | Type of Intervention   | Outcomes   |
|--|--|-----------------------------------|--|--|--|---|--|--|
| 2017 <sup>43</sup><br>2017 <sup>43</sup> | To study the impact<br>of participatory<br>learning and<br>action on<br>maternal and<br>child health<br>outcomes | RCT<br>Cluster                    | India<br>(Jharkhand,<br>Orissa)              | 5781                                     | Pregnant women:<br>3001 infants<br>followed-up for<br>birth outcomes | October 2013<br>to December<br>2015               | BCC:<br>Participatory learning<br>cycle facilitated by<br>su-Poshan Karyakarta<br>(SPK), through women's<br>group meetings, review<br>meetings, home visits,<br>monitoring, and referral<br>services   | Maternal BMI (9 months<br>postpartum):<br>No significant difference (0.186;<br>95% Cl, $-0.025$ , 0.397;<br>P = 0.08)<br>Maternal MUAC at third<br>trimester:<br>No significant difference (0.012;<br>95% Cl, $-0.154$ , 0.179;<br>P = 0.038)<br>Birthweight:<br>No significant difference<br>Women attaining MDD:<br>Significantly higher in the<br>intervention group (OR<br>1.39; 95% Cl, 1.03, 1.90;<br>P = 0.0311)<br>Mothers' hygiene practices:<br>More mothers practised<br>handwashing before eating<br>(OR 5.23; 95% Cl, 2.64, 10.5;<br>P < 0.0001)<br>Child underweight at<br>1.8 months:<br>Significantly reduced odds (OR<br>0.81; 95% Cl, 0.66, 0.91;<br>P = 0.0436) |
| bbreviations:<br>/ height in me          | : BCC, behavior change c<br>eters squared): GLV, gree  | ommunication;<br>:n leafy vegetab | BEP, balanced energ)<br>les; Hb, hemoglobin; | / protein; BINP, B<br>IFA, iron-folic ac | angladesh Integrated Nu<br>id; IoM, Institute of Med                 | utritional Program; BN<br>licine; LAZ, length for | Abbreviations: BCC, behavior change communication; BEP, balanced energy protein; BINP, Bangladesh Integrated Nutritional Program; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); GLV, green leafy vegetables; HD, hemoglobin; IFA, iron-folic acid; IoM, Institute of Medicine; LAZ, length for age Z score; LBW, low birth weight; LNP, lipid-based nutrient | as weight in kilograms divided<br>eieht: LNP libid-based nutrient  |

supplement; MDD, maternal dietary diversity; MINIMat, Maternal and Infant Nutrition Interventions in MATLAB; MUAC, Mid-upper arm circumference; NNP, National Nutrition Program; RCT, randomized controlled trial; UNIMMAP, UNICEF/WHO/United Nations University multiple micronutrient preparation; WAZ, weight for age Z score; WLZ, weight for length Z score.

study was included in the analysis.<sup>31-34</sup> The study by Matias et al.<sup>31</sup> in rural Bangladesh (Rang-din study), with 26% of the participants with BMI <18.5, reported no difference in overall outcomes (maternal anthropometric outcomes such as weight gain and MUAC) in the two groups (women receiving lipid-based nutrient supplements for pregnant and lactating [LNS-PL] and IFA supplements). In a subgroup with multiparous women aged 25 years and older, LNS-PL supplementation contributed to a greater weight gain (34 g/week, P = 0.001) and higher MUAC (+0.4 cm, P = 0.003) than the participants in the IFA group (P = 0.001). In a second subgroup of women with baseline height at the lowest quartile of the distribution, LNS-PL supplementation led to a 0.1-0.3 cm higher MUAC at 36 weeks of gestation compared with the IFA group (P = 0.004 - 0.014). In the entire sample, the participants in the LNS-PL group reported a weight gain of approximately 6.8 kg over 23 weeks, which was still below the recommended guidelines for GWG during pregnancy.<sup>31</sup>

In a multicountry study, Hambridge et al.<sup>32</sup> administered LNS (to all women) arm 1 at ≥3 months before conception and arm 2 late in the first trimester, and in addition arm 1 and 2 with BMI <20 (>90% of women) were also provided a protein-energy supplement. Arm 3 was the control group with no supplements. The authors found that the intervention initiated in the preconception period or during the first trimester, compared with arm 3, resulted in increased birth size and reduced rates of stunting, wasting, underweight, and SGA. The overall mean length-for-age Z score at birth was higher in the first arm (women receiving supplement from ≥3 months before conception to delivery) (P < 0.01), although nonsignificant effect was observed for the Indian cohort (+0.17; 95% CI, P = 0.1244). LBW was reduced in the first and second arm (women receiving supplements from the second trimester onward): RR 0.86: 95% CI. 0.75-0.98: P = 0.026 and RR 0.81; 95% CI, 0.70-0.93; P = 0.004, respectively. Arm 1 had greater weight gain at both 12 weeks (0.8  $\pm$  3.9, 0.0  $\pm$  3.8, and  $0.3 \pm 3.7$  kg in first, second, and third arms respectively; P < 0.001) and 32 weeks (6.9  $\pm$  4.5, 6.4  $\pm$  4.1, and 6.2  $\pm$  4.4 kg in first, second, and third arms respectively; P < 0.001) of gestation compared with arms 2 and 3. The overall compliance was 87.2% for the LNS and 84% for the BEP supplement.<sup>32</sup>

The Bangladesh MINIMat (Maternal and Infant Nutrition Interventions in MATLAB) study involving two food groups (early invitation to food supplementation and usual invitation to food supplementation) and three micronutrient groups (different dosages of IFA: Fe30F, Fe60F, and MMNs, as per UNIMMAP) resulting in six groups in all.<sup>33</sup> Overall, 27.4% in the early food supplementation group and 27.7% in the usual food supplementation group had BMI <18.5. There was no significant difference among the groups in terms of birth weight, birth length, head circumference, fetal loss, and perinatal mortality. The MMN group with early food supplementation had reduced rates for neonatal mortality (HR 0.31; 95% Cl, 0.13-0.72), infant mortality (HR 0.38; 95% Cl, 0.18-0.78), and under-5 mortality rate (HR 0.38; 95% CI, 0.18-0.78). However, the usual food supplementation with MMN group had the highest incidence of infant mortality, although the hazard ratio estimates did not reach statistical significance.<sup>33,34</sup>

### 3.4 | Nutrition education

Two studies evaluating the impact of nutrition education on the impact of nutritional status of pregnant women in India were identified.<sup>35,36</sup> Garg and Kashyap<sup>35</sup> reported improvement in the quality and quantity of dietary intake (P < 0.001 for milk, cereals, green leafy vegetables, fruits, and fat; P < 0.05 for pulses, roots, and tubers) and nutrient intake (P < 0.001 for all nutrients) among mothers after counselling. However, improvement in maternal weight gain per week (0.40 kg) was not significant compared with control.<sup>35</sup> The study by Daniel et al.<sup>36</sup> reported significantly higher weight gain in the intervention group (8.8  $\pm$  2.0 kg) compared with the control group (6.9  $\pm$  1.4 kg; P < 0.0001) with only education. However, no significant difference in birth weight was observed.<sup>36</sup>

### 3.5 | Combined BEP supplementation and nutrition education

Five studies involving 3027 women reported the use of nutrition education and BEP as interventions during pregnancy.<sup>37-41</sup> All studies were from Bangladesh, with observational cohorts from the Bangladesh Integrated Nutrition Project (BINP), later known as the National Nutrition Program (NNP). Only one study reported an increase in weight gain during pregnancy with 69.5% (as opposed to 49% in the control group, P = 0.004) of mothers in the intervention group having appropriate weight gain (>7 kg).<sup>37</sup> Studies by Karim et al.<sup>41</sup> and Shaheen et al.<sup>39</sup> reported a lower prevalence of LBW babies and increased birthweight. Shaheen et al.<sup>39</sup> found a doseresponse relationship for an increase in birthweight (1 g/day for each day of supplementation, P = 0.007). In subgroup analyses, the authors reported an increase in birthweight of 3 g/day of supplementation for women with postpartum weight above 42 kg and an increase of 1.8 g/day of supplementation for pregnant women adhering to the supplements for more than 4 months during pregnancy. In the study by Nahar et al.,<sup>40</sup> neither mean weight gain during pregnancy nor prevalence of LBW was significantly different between intervention and control groups.

### 3.6 | Behavior change communication

Two studies from Nepal and India involving 30 873 women reported outcomes on BCC.<sup>42,43</sup> The community-based participatory learning and action (PLA) study by Saville et al.<sup>42</sup> reported significantly higher birthweight by 78 g (95% Cl, 13.9–142.0; P = 0.0143) in the group that received both PLA and BEP supplementation compared with the control arm that received usual government services. Weight gain during pregnancy was also higher in all three intervention groups than in the control group, although it was not significant. There were no other significant differences observed in maternal and child anthropometry. In the PLA groups, supplemented with food or cash, almost 94%–97% of women attended the group

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meetings regularly, while in the PLA only group the compliance was only 49%.  $^{\rm 42}$ 

In a large cohort study of pregnant women from Jharkhand and Odisha, the PLA was facilitated by community volunteers (*Suposhan Karyakarta*); there were no significant differences in the primary outcomes of interest, but mothers in the intervention group had a significantly higher chance of attaining minimum dietary diversity (OR 1.39; 95% CI, 1.03–1.90; P = 0.0311) and better hygiene practices.<sup>43</sup> Significantly reduced odds of the child being underweight at 18 months of age was also observed (OR 0.81; 95% CI, 0.66–0.91; P = 0.0436) in the intervention group.<sup>43</sup>

### 3.7 | Strategies adopted by other South Asian countries to manage maternal severe thinness

Maternal nutrition interventions are covered under larger health and nutrition programs in South Asian countries (Table 2). Sri Lanka and Nepal are the only two countries in the region to manage maternal thinness in their country guidelines for field health workers.<sup>47,48</sup> In Sri Lanka, assessment of maternal nutritional status using prepregnancy BMI is mandatory. Any pregnant women with BMI <18.5 or inadequate weight gain (<1 kg/month) is enlisted for a special service package that includes assessment of calorie, protein, and micronutrient intake using 24-h dietary recall; assessment of dietary habits, food taboos, misconceptions; nutrition counseling on increasing the amount of starch-based

foods at each meal, consuming 1-2 extra meals than usual, using 1-2 tablespoons of oil and including fish/dried fish/egg, pulses, vegetables, and green leaves to the daily diet; dietary supplementation with two packets of Thriposha (each packet 750 g) monthly (50 g/day to be consumed with two teaspoons each of sugar and coconut; (401.8 kcal, 61.9 g carbohydrate, 20 g protein, 18 mg iron); and follow-ups to assess compliance and, as for other pregnant women, prevent anemia including IFA supplementation and deworming. Thin pregnant women and their husbands/other family members are counselled on non-diet related themes, including reducing workload, mental relaxation, fetal well-being, limiting exposure to household smoke and passive tobacco smoke, and examining for any other illnesses in mothers such as urinary tract infections, parasitic infections, and medical illnesses (hypertension, diabetes). If weight gain continued to be inadequate, pregnant women were referred to a higher health facility.47

In Nepal's Integrated Management of Acute Malnutrition (IMAM) guidelines,<sup>48</sup> pregnant women (second and third trimester) and lactating women (children under 6 months) with MUAC less than 23 cm are nutritionally managed by; (a) Nutrition counselling on use of locally available foods, preparation and intake of high energy-dense meals—such as *Sarbottam Pitho*, a locally developed "super flour"—to provide extra daily nutrient requirements, provision of MMNs to fortify foods at home; (b) In areas where local food availability and access are not sufficient to improve nutritional status, provision of 200 g of dry matter of fortified blended foods per day made from a mixture of corn,

TABLE 2 Policies and programs covering maternal nutrition, listed by countries in South Asia

| Country    | Policies and programs  |
|------------|--|
| Nepal      | The Multi-Sector Nutrition Plan (MSNP-II, 2018–2022), focusses on multisectoral nutrition-specific and<br>nutrition-sensitive programming in the country involving a "Common Results Framework" for monitoring<br>and evaluation   |
| Bangladesh | The second National Plan of Action on Nutrition (NPAN-2, 2016–2025) in Bangladesh involves a set of<br>interventions for the first 1000 days, through the National Nutrition Service. For effective delivery and<br>program evaluation, District Health Information System 2 (DHIS-2) has been developed   |
| Sri Lanka  | <ul> <li>Major policies and programs include the National Nutrition Policy (2010), National Policy on Maternal and Child Health (2012), and the National Strategic Plan on Maternal and Newborn Health (2017-2025)</li> <li>Platforms for antenatal and postnatal care exist through health sectors and social protection (food supplement known as Thriposha, special maternity food for 6 months during pregnancy and 4 months after delivery). The food supplement is given to all women, regardless of their nutrition status</li> </ul> |
| Bhutan     | <ul> <li>Food and Nutrition Security Policy (2014) and the National Health Policy of Bhutan (2011) cover comprehensive maternal and child healthcare services.</li> <li>The National Food and Nutrition Security Strategy (2016-2025) and the 12th five-year plan are aligned with the World Health Assembly global targets (2025) for maternal nutrition</li> </ul>   |
| Pakistan   | National Health Vision 2016–2025, includes a 10-point priority agenda and actions for maternal nutrition, and<br>is supplemented by the National Multi-sectoral Nutrition Strategy, National and Provincial Food Fortification<br>Strategy, Punjab and Sindh Stunting Reduction Framework  |
| Maldives   | <ul> <li>Maternal nutrition actions are covered through the National Reproductive Health Strategy (2014–2018),<br/>Integrated National Nutrition Strategic Plan (2013–2017), Multi-sectoral Action Plan for the Prevention and<br/>Control of Non-Communicable diseases (2014–2020)</li> <li>The government has also developed a Social and Behavior Change Communication (SBCC) strategy focused<br/>on the first 1000 days</li> </ul>  |

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wheat, rice, soya, milk powder, sugar, oil, vitamins, and minerals (787 kcal, 33 g protein [17%], 20 g fat, essential fatty acids and all the required micronutrients), along with counselling on use of supplementary food.

## 3.8 | Current policy, financial, and programmatic gaps to prevent, screen, and manage maternal severe thinness

A comparison of India's ANC nutritional interventions with global recommendations is presented in Table 3.

WHO recommends using pre-pregnancy BMI and MUAC to screen pregnant women for thinness and severe thinness.<sup>49</sup> The BMI cutoffs for classifying thin, normal, overweight, and obese women were reviewed for Asian populations but remained unaltered for screening thin (any form) and severely thin women at BMIs of 18.5 and 16, respectively.<sup>23,24</sup> WHO recommended the development of country-specific cutoffs for MUAC.<sup>45</sup> A review of Indian studies on pregnant and nonpregnant women suggests MUAC <23 and <21 cm or <19 cm correlates with thinness (any form) and moderate to severe thinness, respectively.<sup>50,51</sup> This corresponds with guidance from the Government of India (GoI) by including guidelines on the management of undernutrition in pregnant women affected by tuberculosis.<sup>23,52</sup> However, MUAC is still to be introduced for universal screening of thin and severely thin pregnant women.

Gol's Nutrition Mission (2018-2022) advocates for intersectoral collaboration, BCC, and counselling focused on health and nutrition services for the first 1000 days; it does not have a defined target for reducing maternal thinness.<sup>53</sup> The WHO has placed substantial emphasis on nutrition assessment and provision of a set of nutrition interventions including provision of balanced energy protein supplementation, iron folic acid (IFA), and calcium supplementation, deworming, GWG monitoring and counselling on nutrition, family planning, and breastfeeding, coupled with efforts to prevent and treat maternal infections and anemia. In India, schemes to deliver the above-mentioned WHO recommendations exist through the government Integrated Child Development Scheme (ICDS) and through the health system under the National Health Mission. However, comprehensive maternal nutrition assessments to identify those who are at nutritional risk and to manage such risks are not available. Largely, apart from anemia, such algorithms are not tested at scale in public health settings. Comprehensive nutritional assessment for risk classification is not being undertaken in routine ANC and customized counselling is not provided, the latter being a recommended service along with nutrition assessment and others as per WHO ANC 2016 guidelines. In India, management of maternal thinness does not feature in any national policy targets, except where there are specific existing comorbidities like tuberculosis, where F100 feed is recommended to undernourished pregnant women with tuberculosis for recovery of lost weight and lean body mass.<sup>23</sup>

Nutrition interventions for all women and children are delivered through the supplementary nutrition program under the ICDS, which reaches out to approximately 19 million pregnant women and lactating mothers and 82 million children aged under 6 years.<sup>54</sup> Services currently include take-home supplementary food (providing 600 kcal, 18–20 g protein, and half the RDA for nine essential micronutrients) and hot cooked meals, health and nutrition education, and health check-ups delivered at *Anganwadi* or home. Table 4 provides a detailed description of the different kinds of supplementary food provided through different government programs.

There have been efforts to develop and test an algorithm with five action points by the National Centre for Excellence and Advanced Research in Diets (NCEARD) in collaboration with several development partners for strengthening nutrition services in routine ANC services in India at facility and community level.<sup>55</sup> As per this algorithm, nutrition assessment of all pregnant women, followed by provision of micronutrient supplements, deworming tablets and insecticide-treated bed-nets (malaria endemic areas only), gestational month-specific counseling, classification of nutrition risks, and then nutrition risk-specific counseling and support/referral. For maternal thinness, screening criteria included BMI <18.5 (<20 weeks of gestation), weight <45 kg or MUAC <23 cm, or GWG <1 kg/month (after first trimester). For severe thinness, screening criteria included MUAC <21 cm or BMI <16. Management options for thinness included individual counseling on diet for 15 min using at-risk cards and the Thali model (a counselling tool consisting of standardized meal menus from breakfast to dinner) after ANC check-up, and checks for co-existence of medical illness and referral for appropriate medical care in both facility and community settings; a red mark on the MCP card for fortnightly follow-up visits in facility settings; and special fortnightly group antenatal counselling using at-risk cards along with food demonstration sessions using standardized recipes by ASHA in the community setting. For severe thinness, in addition to the above-mentioned thinness management options, linkage for additional snacks (additional 700 kcal and 35 g protein) through statespecific schemes was advised, with additional follow-up fortnightly home visits by ASHA in both community and facility settings. This was implemented in different parts of India including New Delhi, Haryana, Kanpur, Madhya Pradesh, Bihar, Ranchi, Telangana, and Mangalore across primary health centers, community health centers and tertiary hospitals between 2018 and 2019. The algorithm was also tested for practical feasibility of layering the MN services in routine settings in Nutritional Rehabilitation Centre (NRC) in Delhi from January 1, 2019 to August 31, 2019, and findings indicated that existing staff were able to deliver the MN service package within the time, cost, and regime of the routine NRC.<sup>56</sup>

As per policymakers" and implementers' experiences and perspectives, there are several challenges in implementing these actions in the facility or community setting (Table 5).

### 4 | DISCUSSION

This desk review explored the effect of nutritional interventions to manage severe thinness among pregnant women for maternal

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TABLE 3 Maternal nutrition interventions recommended by WHO (2016), SAARC regional maternal nutrition guidance (forthcoming), and those covered under national programs/guidelines of India

| S. No. | WHO recommendation   | Covered in national guidelines,<br>India  | Not covered in national<br>guidelines, India                               |
|--------|--|---|--|
| 1      | Nutritional screening (prepregnancy BMI, height, weight gain, anemia screening etc)  | Nutritional screening includes<br>gestational weight gain and<br>anemia   | Prepregnancy BMI is not<br>covered. Height is not<br>measured consistently |
| 2      | Counselling on healthy eating and physical activity to stay healthy and prevent excessive weight gain  | Counselling covered but<br>messaging for healthy eating<br>and physical activity not<br>standardized  | -  |
| 3      | Counselling on increasing daily energy and protein intake<br>for women who are severely thin to reduce risk of LBW<br>(context specific)   | -   | No customized counselling<br>for severely thin pregnant<br>women           |
| 4      | IFA supplementation  | Daily IFA supplements (60 mg<br>elemental iron and 500 µg<br>folic acid) recommended<br>14 weeks onwards for<br>180 days and 180 days<br>postpartum. Folic acid 400 µg<br>recommended pre-pregnancy<br>and in first trimester | IFA in first trimester of pregnancy  |
| 5      | Calcium supplementation (context specific)   | Dietary calcium supplementation<br>(500 mg twice a day)<br>recommended to reduce<br>pre-eclampsia and preterm<br>birth risk 14 weeks onward<br>for 180 days and 180 days<br>postpartum  | -  |
| 6      | Vitamin A supplementation (context specific)   | -   | Not recommended  |
| 7      | Balanced protein–energy supplementations (context specific)  | Balanced energy and protein<br>dietary supplementation<br>through Anganwadi services  | -  |
| 8      | Restriction of caffeine intake (context specific)  | -   | No advice or counselling on<br>restriction of caffeine intake              |
| 9      | Counselling on early and exclusive breastfeeding   | Counselling covered with<br>standard messaging on early<br>and exclusive breastfeeding<br>under MAA program   | -  |
| 10     | Prevention and management of infectious diseases such<br>as soil-transmitted helminths and malaria (context<br>specific)   | Maternal deworming with single<br>dose of 400 mg albendazole<br>recommended in second<br>trimester<br>Provision of insecticide treated<br>bed nets for prevention of<br>malaria in endemic areas                              | -  |
| 11     | -  | Promotion of iodized salt and/or<br>double fortified salt   | -  |
| 12     | -  | Linkage to government schemes<br>for access to free drugs,<br>diagnosis, nutritious diet,<br>referral, institutional<br>deliveries at all public health<br>facilities   | -  |
| 13     | Use of F75 or F100 therapeutic milk products designed to<br>treat severe malnutrition for adolescents and adults<br>(ingredients include concentrated milk powder, food oil,<br>and dextrin vitamin complexes. The designations mean<br>that the products contain 75 and 100 kcal per 100 ml,<br>respectively) | Among pregnant women<br>affected by tuberculosis,<br>management as per WHO<br>guidelines is recommended,<br>followed by food support  | No interventions for severely<br>thin women with no medical<br>comorbidity |

Abbreviations: BMI, body mass index; IFA, iron-folic acid; LBW, low birth weight; MAA, Mother's Absolute Affection.

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TABLE 4 Different types of supplementary food provided across the states in India

| Name of supplementary  |                     |   | Energy,<br>kcal | Protein, g | Fats, g |
|--|---------------------|---|-----------------|------------|---------|
| food   | State               | Composition   | Per 100 g       |            |         |
| 1. Amrutham Nutrimix   | Kerala              | Wheat, soya chunks, Bengal gram, groundnut,<br>sugar  | 391             | 16.14      | 69.47   |
| 2. PWLMAG  | Kerala              | Wheat, white rice, ragi, Bengal gram, green gram, soya chunks                                   | 501             | 23.3       | 5.9     |
| 3. Shakti Nutrimix   | West Bengal         | Rice, wheat, whole gram (chana), groundnut, sugar   | 402             | 10.4       | 5.3     |
| 4. Chhatua   | Odisha              | Wheat, roasted chana, groundnut, sugar  | 303             | 11.7       | 5.68    |
| 4. Complementary food<br>containing amylase<br>activity        | Tamil Nadu          | Wheat, ragi, Bengal gram, dhal flour  | 330             | 8.99       | 1.58    |
| 5. Fortified Sukhadi<br>Premix                                 | Maharashtra/Gujarat | Whole wheat flour, Defatted soya flour, edible oil, jaggery, groundnut                          | 463             | 15.06      | 23.14   |
| 6. Fortified Sheera Premix                                     | Maharashtra/Gujarat | Atta, full fatted soya flour, green gram, sugar, edible oil, groundnut                          | 455             | 16.52      | 27.8    |
| 7. Fortified Upma Premix                                       | Maharashtra/Gujarat | Whole wheat flour, full fatted soya, green gram,<br>edible oil, groundnut, coconut oil, sugar   | 462             | 11.8       | 30.42   |
| 8. Energy dense extruded fortified Halwa premix                | Rajasthan           | Whole wheat, defatted soya bean, green gram,<br>edible oil, sugar, micronutrients (as per norm) | 344             | 12.65      | 17.27   |
| 9. Arogya Lakshmi, one full<br>meal scheme (per meal)          | Telangana           | Rice, dal, vegetables, milk, egg, oil   | 1192.38         | 37.04      | NA      |
| 10. Mathrupoorna, one full<br>meal scheme (per meal)           | Karnataka           | Rice, dal, vegetables, milk, egg, oil, peanut chikki  | 1342.38         | 41.04      | NA      |
| 11. Anna Amrutha<br>Hastham one full meal<br>scheme (per meal) | Andhra Pradesh      | Rice/wheat/millets, dhal, oil, milk, vegetables, condiments                                     | 1052.7          | 32.8       | NA      |
| 12. Mahatri Jatan Yojana<br>(per meal)                         | Chhattisgarh        | Rice, soya oil, mix dal, vegetables   | 914             | 21         | NA      |

and childhood outcomes. Results suggest that BEP supplementation with or without a nutrition education component appears promising; however, the type of supplement varied across the studies to preclude any conclusive recommendation. Nonetheless, it emerged that a longer duration of supplementation, preferably starting with preconception, may have a better impact on both pregnancy weight gain and reducing LBW. The longer-term benefits of BEP or MMN supplementation in terms of child growth post-infancy were not evident from the trials/observational studies available. Both nutrition education and more intensive behavior change strategies appeared to influence diet-related behaviors but not maternal or newborn nutritional outcomes. Compliance to BCC through PLA was more effective when either cash or supplements were provided. None of the studies we reviewed covered findings for pregnant women who were severely thin. Among South Asian countries, Sri Lanka and Nepal were the only two countries to have guidance on community management of thinness in pregnancy. The package in Sri Lanka included prepregnancy BMI as a criterion for screening thin women, enlisting them for closer follow-up and extra supplementary food (Thriposhan) for all thin pregnant women. Nepal's IMAM guidelines recommend that pregnant and lactating women should take with MUAC <23 cm should take 200 g of dry matter of fortified blended food per day to improve nutritional status. In India, at least nine variations of supplementary food—specific to local food choices in states—are available, and three states (Andhra Pradesh, Karnataka, and Telangana) also have a full meal plan.

A recent review of South Asian programs that strengthen maternal nutrition services listed only one study on strengthening nutritional counselling to improve quantity and diversity of food intake, while eight were on IFA supplementation.<sup>57</sup> There are many commonalities between the proposed five action point maternal nutrition algorithm and what is being done in Sri Lanka. The proposed five action points for maternal nutrition, including management of severe thinness, are being rolled out in five Indian states. The evidence presented in this article and experience from state roll-out of maternal nutrition services paves the road ahead for further strengthening of the five action point maternal nutrition algorithm, especially management of severe thinness. Based on this review, the following recommendations are put forward:

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### 4.1 | Recommended actions

 Promote the inclusion of BMI-based screening for thinness (BMI <18.5) and severe thinness (BMI <16) for all pregnant women contacted within the first trimester by a health service provider (Auxiliary Nurse Midwife, Community Health Officer, Nursing staff or Medical Officer) and no weight gain or weight gain <1 kg per month after the first trimester or weight <45 kg at any contact may be considered a highrisk indicator. Such women are at nutrition risk, and will require counseling and/or food supplementation. However, BEP supplementation with nutrition education is promising but needs to be carried out for a longer duration starting with pre-conception and at scale.

TABLE 5 Current status and gaps in implementing five actions for maternal thinness and severe thinness per the algorithm developed and tested by the Government of India, experts, development partners and NCEARD

| Pillars   | Status  | Gaps   |
|---|---|--|
| <ol> <li>Implementation guidelines availability and<br/>accountability</li> </ol> | <ul> <li>Maternal nutrition guidelines tested and available for roll-out<br/>Resources available include:<br/>Algorithm (five actions) for facility and community level<br/>Flipbook for group counselling<br/>By-gestational month cards for group counselling<br/>At-risk cards/condition-specific cards for individual counselling<br/>Recipe book on nine conditions<br/>BMI chart for field workers<br/>CAPI-based tool on CSPro for data entry<br/>Maternal nutrition guidelines rolled out<br/>in: Bihar, Delhi, Jharkhand, Madhya<br/>Pradesh</li> <li>Specific components of these guidelines<br/>are already included in national programs<br/><i>Surakshit Matritva Aashwaasan</i><br/>(SUMAN), Ministry of Health and<br/>Family Welfare: Recipe book on nine<br/>conditions, Thali models (normal<br/>weight, thin, obese and anemic),<br/>Leaflet for pregnant women (normal<br/>weight, thin, obese and anemic), by-<br/>gestational month cards, flipbook<br/>Ministry of Woman and Child<br/>Development: Regional recipes leaflet<br/>for pregnant women (normal weight,<br/>thin, obese, and anemic) in North,<br/>North-East, Central, West, and South<br/>regions</li> </ul> | <ul> <li>Lack of gestational weight gain<br/>charts and corresponding optimal<br/>weight gain. Standard of 10–12 kg<br/>being followed without base<br/>weight reference point.</li> <li>ANMS, MOs, and specialists<br/>undertook nutrition assessments<br/>and actions but neither<br/>consistently nor comprehensively<br/>done (weight measurement and<br/>hemoglobin assessment most<br/>frequently done)</li> </ul> |
|   | ✓ Micronutrients covered under guidelines:<br>iron, folic acid, calcium, iodine, vitamin D  | ✓ Emerging micronutrient<br>deficiencies: vitamin B6, B12,<br>and Zinc unaddressed in draft<br>guidelines  |
|   | ✓ Guidelines: gestational diabetes,<br>tuberculosis, and HIV have a nutrition<br>component  | <ul> <li>Guidelines on thyroid disorders<br/>that are now commonly reported<br/>in pregnancy (and other medical<br/>conditions) need to have a<br/>nutrition management section</li> </ul>   |
|   | <ul> <li>Roles and accountability for preventing<br/>and managing maternal malnutrition<br/>defined in draft guidelines (Facility:<br/>ANM, CHO, and MO; Community: ANM,<br/>ASHA, and AWW)</li> </ul>  | <ul> <li>Available nutrition norms need<br/>to penetrate the service delivery<br/>system (increase provider<br/>awareness)</li> </ul>  |
|   |   | (Continues)  |

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### TABLE 5 (Continued)

| Pillars                      | Status  | Gaps   |
|------------------------------|---|--|
| 2. Plans and financing       | <ul> <li>Budget Head available under National<br/>Health Mission:</li> <li>Procurement (IFA, calcium, albendazole,<br/>iron, sucrose and hemoglobinometer)</li> <li>ASHA Incentive (mobilizing lactating<br/>women under Anemia Mukt Bharat)</li> <li>Capacity building under Maternal Health<br/>Strengthening maternal health service<br/>(community-based, facility-based,<br/>JSSK diets etc)</li> <li>IEC/SBCC</li> <li>Printing</li> <li>Flexibility under each head</li> </ul> | <ul> <li>Heads available but budget<br/>amounts need to match<br/>requirements for training,<br/>outreach, equipment, and supplies.<br/>The gaps vary by state; however,<br/>there was a significant planning<br/>gap of 73% in 14 states' analyses</li> <li>Capacity building (maternal<br/>nutrition training with estimated<br/>cost needs to be incorporated<br/>within the available budget heads)</li> <li>Maternal nutrition IEC/SBCC and<br/>printing activities need to be listed<br/>and costed</li> </ul> |
| 3. Demand creation           | Standard communication/counselling<br>materials for pregnancy nutrition,<br>nutritional disorders, and nine medical<br>comorbidities available but yet to be<br>rolled out  | <ul> <li>Stakeholder consensus on<br/>consistency in using messages<br/>across regions and platforms (with<br/>localization as needed)</li> <li>Engagement of private sector<br/>providers in demand creation</li> </ul>   |
| 4. Leadership and governance | Poshan Abhiyaan targets being closely<br>monitored  | <ul> <li>Overweight/obesity through life<br/>course (or at any specific stage in<br/>life course) is missed in the Poshan<br/>Abhiyaan targets</li> <li>Management strategies for<br/>thin and obese women require<br/>coordination across Woman<br/>and Child Development, Rural<br/>Development, and other<br/>departments</li> <li>Review of maternal nutrition<br/>initiatives within Poshan Abhiyaan</li> </ul>   |
| 5. Partnerships              | <ul> <li>✓ Maternal nutrition consortium created</li> <li>✓ NCEARD established to forge national<br/>and regional partnerships</li> </ul>   | <ul> <li>Models for engaging private sector<br/>providers needed</li> <li>Regional centers of excellence on<br/>maternal nutrition needed through<br/>government or corporate funding<br/>support</li> </ul>   |
| 6. Information systems/M&E   | The RCH portal and HMIS combined covers<br>monitoring targets for maternal anemia<br>(process and outcome level)<br>Maternal nutrition scorecards based on<br>HMIS Indicators have been developed   | Indicators for BMI based tracking and counselling services needed  |
| 7. Capacity building         | <ul> <li>✓ Training resources are available and<br/>rolled out in four states (Bihar, Delhi,<br/>Jharkhand, Madhya Pradesh)</li> <li>✓ Master trainers:<br/>Madhya Pradesh: 410<br/>Bihar: 40<br/>Jharkhand: 187<br/>Delhi: 131</li> </ul>  | Identify platforms where half-day<br>trainings on maternal nutrition for<br>ASHA, AWW, ANM, MO, CHO<br>can be integrated (state level)   |
| 8. Supply                    | <ul> <li>✓ Equipment available: digital weighing<br/>scale</li> <li>✓ Medicines/supplements: folic acid<br/>tablets, IFA, iron sucrose, calcium<br/>tablets, albendazole, glucose load</li> </ul>   | <ul> <li>✓ Equipment needed: stadiometer,<br/>nonstretchable inelastic tape,<br/>hemoglobinometer</li> <li>✓ Procurement challenges for<br/>medicines/supplements</li> </ul>   |
| 9. Institutional mechanism   | NCEARD technical support unit for<br>maternal nutrition   | Regional centers needed  |



| Pillars                          | Status  | Gaps   |
|----------------------------------|---|--|
| 10. Research and policy dialogue | <ul> <li>Consultation meetings (13) to develop<br/>the maternal nutrition guidelines,<br/>algorithms, and communication materials</li> <li>Maternal Nutrition symposium series<br/>planned with themes: severe thinness,<br/>obesity, anemia, and depression</li> <li>Results from the management of<br/>severely thin pregnant women and<br/>mothers at Nutrition Rehabilitation<br/>Centers will be available soon</li> </ul> | <ul> <li>GWG monitoring charts for<br/>normal, thin, and obese pregnant<br/>women</li> <li>Managing gestational weight in<br/>thin and obese mothers</li> <li>Operational models where<br/>thinness and obesity are managed<br/>through health systems (engaging<br/>health and wellness centers)</li> <li>Multiple micronutrient<br/>supplements vs IFA in thin<br/>pregnant women</li> </ul> |

Abbreviations: ANM, Auxiliary Nurse Midwife; ASHA, Accredited Social Health Activist; AWW, Anganwadi Worker; BMI, Body Mass Index; CHO, Community Health Officer; HMIS, Health Management Infornation System; IEC, Information, Education and Communication; IFA, iron-folic acid; JSSK, Janani Shishu Suraksha Karyakaram; MO, Medical Officer; NCEARD, National Centre of Excellence and Advanced Research on Diets; RCH, Reproductive Child Health; SBCC, Social and Behavioral Change Communication.

- Efforts should be made to ensure pregnant women are registered as early as possible within the first trimester and linkage preconception and maternal nutrition in pregnancy programmes is there for ensuring continuity of interventions.
- 3. Districts with the highest number of severe thinness cases in pregnancy and postpartum require closer review of maternal nutrition services in these areas, for strengthening and testing 5-actions under the algorithm at scale for feasibility and effectiveness across all platforms—facility and community. Simultaneously, efforts will be needed to address systems bottlenecks that impede implementation such as gaps in capacities of health providers especially in counselling, equipment supplies, incentives, supervision, monitoring and data-driven review.
- 4. Nutrition assessment and classification of nutrition risks has its challenges of data points, early enrolment, construct validity and time available with worker. Indian government has initiated programme feasibility—five integrated actions using a systems approach. This must be documented. Ongoing health systems/ social protection systems research on maternal nutrition must be replicated for feasibility and long-term implications.

### 5 | CONCLUSION

More implementation research is needed to develop a standard service delivery package to manage severe thinness as medical nutrition therapy, some of which is ongoing in selected health facilities, NRCs, and community settings. Guidelines from neighboring Sri Lanka, drivers of maternal severe thinness, and successes (albeit limited) from intervention trials provide evidence for promoting a combination of interventions including comprehensive nutritional assessment and follow-up, diet and related counselling and nutrition education, and in some cases additional dietary supplementation.

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### CONFLICTS OF INTEREST

The authors have no conflicts of interest.

### AUTHOR CONTRIBUTIONS

VS and AB conceptualized the paper and drafted it with contributions from TC. All other authors reviewed the manuscript and contributed to the interpretation of findings. All authors agreed the final version of the paper.

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