Abstract

Background. Stunting, acute malnutrition, and micronutrient malnutrition are persistent public health problems in refugee populations worldwide. In recent years there has been an increase in the availability and use of special nutritional products in emergency and development contexts to help address inadequate nutrient intakes from low-diversity diets. The availability of new special nutritional products, and the decision by the United Nations High Commissioner for Refugees (UNHCR) to use blanket supplementary feeding programs to prevent stunting and anemia, raised new challenges for designing, monitoring, and evaluating nutritional programs.

Objective. To develop an Operational Guidance on the use of special nutritional products for the prevention of micronutrient malnutrition, stunting, and acute malnutrition in refugee populations.

Methods. A literature review and a series of consultations with technical experts, operational organizations, and field staff were performed over a period of 2 years. The Operational Guidance was finalized and released in December 2011.

Results. The Operational Guidance describes six stages for defining nutritional problems and identifying possible solutions; assessing and managing risks; testing acceptability and adherence, program design and implementation; and monitoring and evaluation. Key performance indicators are defined and a working nomenclature for new special nutritional products is described.

Conclusions. The UNHCR Operational Guidance has filled an important gap in helping field staff deal with the opportunities and challenges of preventing undernutrition through the use of new products in blanket supplementary feeding programs. The need for further integration of guidance on selective feeding programs is discussed.

Key words: Anemia, lipid-based nutrient supplement, malnutrition, micronutrient deficiencies, prevention, refugees, stunting, wasting

Introduction

Acute malnutrition, stunting, and micronutrient malnutrition are serious public health problems among food aid-dependent refugee populations worldwide, affecting the health and development of young children. These forms of undernutrition have been frequently documented among emergency-affected populations, who often face limited access to diversified diets or livelihood opportunities, poor sanitation and hygiene facilities, and recurrent illness and infection [1–6]. Despite efforts to control and reduce undernutrition in refugee situations, the problem has remained serious [7–10], and the effectiveness of the international aid response in preventing micronutrient deficiencies and malnutrition has frequently been called into question [11, 12].

Health and nutrition statistics from refugee camps illustrate the need for further action, as global acute malnutrition (GAM) (weight-for-height z-score < –2 and/or edema), stunting (height-for-age z-score < –2), and anemia (hemoglobin concentration < 11.0 g/dL) in children aged 6 to 59 months are frequently above the acceptable limits defined by the World Health Organization (WHO) [13, 14]. For instance, between 2007 and 2008, surveys conducted by the United Nations High Commissioner for Refugees (UNHCR) and its implementing partners found that in 10 countries the...
prevalence of anemia in young refugee children was above the WHO cutoff for defining a public health problem (>20%), in eight countries the public health situation was severe (>40%), and in six of these eight countries the prevalence was above 60%, classifying the situation as a public health emergency [15].

Data relating to GAM and stunting are equally concerning. Data from UNHCR’s Health Information System indicate that in many refugee contexts, the prevalence of GAM is frequently above acceptable (5%) and even critical levels (>15%). For example, in 2010, the prevalence of GAM reached 29.5% in camps in Ethiopia, 15.9% in Bangladesh, and 12.8% in Algeria, while the prevalence of stunting was 40.6%, 70.9% and 27.3% respectively [16].

These data suggest that the “typical” general food ration currently provided in emergency settings—based on cereals, pulses, a fortified blended food (FBF), oil, and sometimes sugar—has not met the nutritional needs of groups who are most vulnerable to malnutrition. Although fortification of staple foods has been shown to reduce micronutrient deficiencies in food aid-dependent refugee populations [17, 18] and improved fortified foods are now available, a review by the World Food Programme (WFP) and the Global Alliance for Improved Nutrition (GAIN), published in 2007, indicated that only around 20% of food aid was fortified [19]. In these situations, the use of special nutritional products for young children may be indicated [20, 21]. Home fortification and improved complementary feeding are increasingly recognized as effective methods of improving the nutritional status of vulnerable groups in emergency and development contexts [20, 22, 23].

In order to tackle the challenge of child undernutrition, UNHCR identified the need to mobilize concerted efforts together with partners to strengthen existing public health and nutrition programs and introduce a number of new interventions. While approaches have been established for acute malnutrition for some years, with the latest UNHCR/WFP guidelines on selective feeding being published in 2011 [24], there was no established strategy for micronutrient malnutrition or stunting. Thus, in 2008/09, UNHCR developed and commenced implementation of a strategy aiming to achieve a reduction in micronutrient malnutrition (using anemia as a proxy indicator) [15].

One of the approaches adopted through this strategy is the introduction of new special nutritional products and the distribution of these through blanket supplementary feeding programs (BSFP). Special nutritional products traditionally consisted of FBF, but there have been moves in recent years to introduce micronutrient powders (MNP) and lipid-based nutrient supplements (LNS). The addition of these food supplementation products (FSP) to meals within the recipient household has been referred to as “home fortification.” Together with WFP and various implementing partners, project activities were initiated in seven pilot countries (Algeria, Bangladesh, Djibouti, Ethiopia, Kenya, Nepal, and Yemen), selected on the basis of need and feasibility.

Many of the products and home fortification approaches being adopted are still relatively new, and the evidence base for their efficacy, effectiveness, and cost-effectiveness was evolving. Although the evidence for efficacy against anemia was strong for MNP, there was limited efficacy data available for LNS, and very little effectiveness data for either type of intervention [21, 25, 26]. This reinforced the need for technical guidance and decision support for staff undertaking assessments, setting up and maintaining intervention programs, monitoring and evaluation, and mainstreaming good practice. The need for guidance on expected impacts and on when, how, and for whom the increasing number of products being developed should be used, was also recognized by de Pee and Bloem [20].

UNHCR’s Operational Guidance was developed to help meet these needs and is aimed at health and nutrition staff from UNHCR and partners. It built on the already existing frameworks developed by WFP/Sight and Life in 2008 (Ten Minutes to Learn About Nutrition Programming series) and complements the UNHCR/WFP Selective Feeding Guidelines [24]. The Moderate Acute Malnutrition (MAM) Task Force of the Global Nutrition Cluster has also recently released a draft decision tool for programs designed to treat or prevent MAM, although this does not include anemia as a program initiation criterion and is not specific to refugee contexts [27].

The purpose of the present paper is to provide an overview of the Operational Guidance and its intended use for intervention planning, implementation, and monitoring and evaluation in refugee camp settings. Additionally, some of the key questions and challenges raised during the development of the Operational Guidance are discussed.

Methods

Development of the Operational Guidance took place over a period of 2 years and benefited from a broad range of experience and knowledge contributed by experts, nongovernmental organizations (NGOs), and field-based teams, as well as the participation of refugee community members in pilot studies. Technical staff from a number of organizations (Centers for Disease Control and Prevention, Micronutrient Initiative, Sight and Life, WFP, and independent consultants) took part in a peer-review process, the feedback from which was systematically and carefully considered before finalization of the guidance. Participant feedback from a technical training workshop for key health and nutrition program staff (held in Mombasa, Kenya, in July 2011) also aided refinement of the guidance and helped focus
attention on what was considered programmatically feasible. The Operational Guidance document was finalized and distributed in print and online (http://info.refugee-nutrition.net/home) in December 2011.

Results

Overview of the operational guidance

As shown in figure 1, the finalized Operational Guidance describes six recommended stages for the planning, implementation, and monitoring and evaluation of BSFP aimed at controlling and reducing micronutrient deficiencies and undernutrition in refugee populations. Although the focus of the Operational Guidance is on the use of FSP for children aged 6 to 59 months, it also considers the use of improved FBF and can be adapted for other vulnerable groups such as pregnant and lactating women, adolescent girls, and the elderly.

The Operational Guidance defines FSP as micronutrient-fortified products designed for “point of use” or “home fortification,” i.e., to be added to other foods in the home to improve micronutrient intake and, in some cases, to provide energy. LNS are defined here as lipid-based pastes designed to deliver nutrients to nutritionally vulnerable people. They provide a range of vitamins and minerals as well as energy, protein, and essential fatty acids, thus differentiating them from traditional multiple micronutrient supplements. When used as a home fortificant, LNS are used to provide energy and nutrients that are missing in the diet, i.e., they are intended to complement the pre-existing diet and not replace it.

The Operational Guidance does not cover the treatment of acute malnutrition and therefore does not include guidance on Ready-to-Use Therapeutic Foods (RUTF) for the treatment of Severe Acute Malnutrition (SAM) such as Plumpy’Nut or eeZeePaste, or Ready-to-Use Supplementary Foods for the treatment of moderate acute malnutrition (MAM), such as Plumpy’Sup.

The FSP programs covered in the Operational Guidance are not intended as stand-alone interventions. Key components of the UNHCR nutrition and anemia strategies are to ensure a comprehensive and integrated approach to prevent and treat micronutrient deficiencies and other forms of undernutrition, as well as to measure the impact of interventions [10, 15]. It is anticipated that successful interventions and activities will eventually be integrated into all refugee operations.

The six stages of the Operational Guidance are detailed below. Ideally, the stages should be conducted in chronological order, although some stages are interrelated and may overlap.

Stage 1

Stage 1 is intended to aid health and nutrition staff in defining the nutritional problems that affect children aged 6 to 59 months within the population of interest. Three main indicators are suggested for use in the assessment of nutritional problems for which FSPs may be considered. These are the prevalence of GAM, anemia, and stunting. These indicators have been selected because they help describe major nutritional problems, are widely available, and can be measured during routine nutrition surveys with reasonable accuracy and precision.

In order to classify the severity of the nutrition situation, prevalence estimates should be gathered for the suggested indicators from the latest cross-sectional nutrition surveys conducted in the camp(s) and interpreted using contextual information. A simplified classification table was developed (based on WHO criteria) that categorizes indicators as low, medium, and high (table 1) [14]. High levels of one or more of these indicators suggest that an FSP intervention may be appropriate and readers should proceed to the subsequent stages. The use of these indicators will target interventions toward populations where a significant number of individuals are already affected by one or more forms of malnutrition. However, as described in stage 2, the focus of these interventions is on prevention within the whole population. It should also be noted that this simplified classification was designed to be used to help select appropriate interventions and that it differs slightly from the global classification used by UNHCR for nutrition survey results.

Stage 2

The purpose of stage 2 is to guide, if required, the selection of a potential FSP intervention for nutritional
problem(s) identified in stage 1. A decision tool containing eight scenarios was developed to guide the identification of potential FSP interventions for children aged 6 to 59 months. Each of the first seven scenarios depicts a potential camp context with high prevalence estimates of one or more of the nutritional problems previously identified, i.e., GAM, anemia, or stunting. The eighth scenario portrays a setting where the prevalence of none of the three indicators is high and an FSP intervention is probably not appropriate. It is recommended to select the scenario that best reflects the situation in the camp or camps, carefully consider the context, and then use the possible intervention options that are listed as a basis for decision-making.

Stage 3

The objective of stage 3 is to identify any risks and precautions that need to be considered before commencing an FSP intervention. These risks may include, but are not limited to, adverse effects on other programs, excessive micronutrient consumption, and adverse effects on feeding practices and child health. Suggested solutions are provided for managing each of these potential risks.

Stage 4

Stage 4 is designed to test the acceptability of the selected FSP to potential target populations and their adherence to the recommended dosage. Standard acceptability and adherence materials and tools are provided for use, including a test protocol. The test includes distribution of the FSP to around 120 participants for a minimum of 3 weeks. Data on local eating habits, cultural beliefs, health knowledge, and acceptability and use of the product are collected using quantitative and qualitative methods at baseline, midpoint, and endline. This will help inform the decision about whether the FSP is acceptable to the community and is used correctly and, therefore, whether to proceed with the selected intervention. It will also guide the design of appropriate, context-specific educational campaigns, distribution mechanisms, and FSP packaging.

All acceptability and adherence materials and tools were reviewed by an anthropologist and piloted in refugee contexts in Algeria, Djibouti, and Yemen, before being finalized for inclusion in the Operational Guidance. All reference materials and tools are working documents and will be improved as experiential feedback and knowledge are gained.

Stage 5

Stage 5 is intended to aid in identifying the key components that need to be in place or developed to ensure that the intervention is planned and implemented effectively. Coordination of all actors needs to be ensured by this stage. Further considerations include logistical components, such as ordering of the product, storage, and stock management; training of health workers and staff; and development of a context-specific communication and education campaign and product distribution channels. Relevant tools are provided to aid with both standardization of training and effective community mobilization.

Stage 6

Finally, as with any program, strong monitoring and evaluation should accompany an FSP intervention, particularly due to the new nature of the products being used, and this is documented in stage 6. Minimum reporting requirements are provided that should be adapted depending on individual programming requirements and the products used.

Associated with each of the different stages described above are a number of online reference materials and tools, such as calculation spreadsheets and questionnaire templates. Although many of the tools and reference materials provided are optional, the standard acceptability and adherence tools are required to aid users in conducting the recommended acceptability and adherence tests.

Discussion

In response to the persistently high prevalence of undernutrition observed in refugee contexts, interventions using special nutritional products and home fortification approaches are being piloted at scale by UNHCR and its partners. The development of different types of LNS and improved FBF has increased interest

<table>
<thead>
<tr>
<th></th>
<th>Prevalence %</th>
<th>High</th>
<th>Medium</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAM</td>
<td>≥ 15</td>
<td>Critical</td>
<td>10-14 Serious</td>
<td>5–9</td>
</tr>
<tr>
<td>Anemia &lt; 5 yr</td>
<td>≥ 40</td>
<td></td>
<td>20–39</td>
<td>5–19</td>
</tr>
<tr>
<td>Stunting</td>
<td>≥ 30</td>
<td></td>
<td>20–29</td>
<td>&lt; 20</td>
</tr>
</tbody>
</table>

*a. Based on WHO criteria [13, 14]*
in their potential role in preventing different types of undernutrition in vulnerable groups [28]. The development of the Operational Guidance is a step forward in a rational and standardized approach to the assessment and use of these new special nutritional products.

Development of the Operational Guidance was needed because of the availability of new special nutritional products and, more fundamentally, because of the decision by UNHCR and its partners to extend the scope of traditional BSFP for children. Whereas these had previously focused on the prevention of wasting, the target of BSFP programs was now to also include the prevention and treatment of both mild and moderate anemia and stunting. This shift in approach and the increased focus on preventive measures extended from the recognized need to improve the management and prevention of these forms of undernutrition as well as the availability of specialized products targeting these conditions [20, 29]. Research suggests that prevention is likely to have a greater long-term effect on the reduction of child undernutrition than traditional treatment models, particularly when focused on children under 2 years of age [30].

Although other relevant guidelines are available or currently under development [24, 27], the Operational Guidance focuses on guiding interventions using or intending to use lower-energy fortified products or MNP for BSFP. The Operational Guidance is intended to be adaptable, and the acceptability protocol and other stages can be adapted for use with other types of products and contexts. Additionally, although its focus is on children aged 6 to 59 months, it can be adapted to other vulnerable groups.

The testing of acceptability and adherence is a crucial step in the successful introduction of any health or nutrition intervention but is often not given the attention it requires [29]. The need for cultural acceptability has been demonstrated in various contexts [31], as well as the need to complement this with appropriate behavior change messages (Operational Guidance stage 5), and effective monitoring and evaluation (Operational Guidance stage 6) to facilitate program improvement. The Operational Guidance therefore places special emphasis on these components.

Challenges

During the development of the Operational Guidance, a number of outstanding issues and challenges remained that could not be fully resolved during its preparation.

Iron supplementation in malaria-affected areas

The longstanding controversy on the use of iron supplementation in malaria-endemic areas was one such challenge, as the guidance on this is not yet clear-cut. Expert advice was sought on whether iron and folic acid doses should be modified in currently available LNS and MNP products before use in regions of high malaria transmission. The latest evidence, recommendations, and guidelines regarding this topic were compiled in issues papers and distributed to experts (including the UNHCR Technical Advisory Group and Technical Reference Group) prior to informal meetings to discuss these issues. Based on the available evidence and the expert consensus, the Operational Guidance recommends the reduction of the iron content of MNP in malaria-affected areas and the reduction or removal of folic acid where antifolate malarial drugs are used. In addition, it should be ensured that appropriate malaria control activities are in place, such as diagnosis and treatment of malaria cases, indoor residual insecticide spraying, and distribution of mosquito nets.

Product classification and terminology

With the increasing number of new lipid-based nutritional products being developed for preventing and treating different types of undernutrition, we considered it important that a widely accepted generic nomenclature be established to avoid confusion and potential misuse of products. This need has been recognized, and the 2008 WHO/UNICEF/WFP/UNHCR consultation on the management of MAM in children under five agreed that “there is an urgent need to develop clear terminology for the different specialized foods used to treat moderate malnutrition” [29]. A consistent classification and naming system is needed to capture the sometimes subtle nuances between the different lipid-based products available.

The suitability of a lipid-based paste in preventing or treating wasting, stunting, or anemia is largely determined by the recommended quantity (in grams) or energy (in kilocalories) per daily dose. Lipid-based pastes can be tailored to meet the needs of specific vulnerable groups and programmatic contexts. As shown in Table 2, there are LNS products such as Nutributter that provide a low amount of energy (108 kcal/day) and have been shown to improve linear growth and iron status in infants aged 6 to 12 months [32, 33], and Plumpy’Doz, which provides more energy (250 kcal/day) and has been shown to reduce the incidence of severe wasting in children aged 6 to 36 months [34]. In contrast, therapeutic foods such as Plumpy’Nut provide significantly more energy per day and are used to temporarily replace most or all foods, other than breastmilk, during a child’s rehabilitation from SAM.

For clarity, it was therefore considered appropriate that lipid-based therapeutic pastes that are designed to
provide all of a child’s caloric and nutrient needs should not be labeled as LNS, but rather as lipid-based RUTF. LNS was further divided into the following categories, based on their different recommended dosages and purposes, and builds on suggestions provided by de Pee and Bloem [20] and recent guidance on the treatment and prevention of acute malnutrition [(27):

» Low quantity LNS (≤ 20 g/≤ ~108 kcal per daily dose)

» Medium quantity LNS (21 to 50 g/109 to ~250 kcal per daily dose)

» High quantity LNS (51 to ≤ 100g/~251 to 500 kcal per daily dose)

This classification, however, has yet to be accepted across all the organizations working on these products, and further efforts on harmonizing nomenclature are required.

Integration with selective feeding guidelines
The UNHCR/WFP Guidelines for Selective Feeding are one of the main sources of guidance for setting up and

### TABLE 2. Summary of recently developed FBF and FSP for use in children aged 6 to 59 months

<table>
<thead>
<tr>
<th>Product</th>
<th>Nutritional contents</th>
<th>Target age group (children)</th>
<th>Shelf-life</th>
<th>Product description and examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBF+</td>
<td>Energy (macro-nutrients) and micronutrients</td>
<td>6–59 mo</td>
<td>12 mo</td>
<td>FBF+, e.g., CSB, WSB, and RSB, (also known as SuperCereal) is a food for young children and other vulnerable groups, as well as the general population. Its content of vitamins and minerals has been modified compared with previous formulations. It is recommended as a partial replacement for nutritionally inadequate local diets.</td>
</tr>
<tr>
<td>FBF++</td>
<td>Energy (macro-nutrients) and micronutrients</td>
<td>6–24 mo</td>
<td>12 mo</td>
<td>FBF++, e.g., CSB++, (also known as SuperCereal plus) is a newly developed FBF for infants and young children. It contains milk powder and has a higher energy density than other types of FBF. It is recommended as a partial replacement for nutritionally inadequate local diets for children and to promote weight gain.</td>
</tr>
<tr>
<td>MNP</td>
<td>Micronutrients only</td>
<td>6–59 mo</td>
<td>24 mo</td>
<td>MNP provide no energy (kcal) in the diet. They are usually packaged in individual sachets to provide a dose of selected vitamins and minerals in powder form, to be added to foods directly after cooking. MNP have been shown to be efficacious in treating and preventing anemia. Product brand names include Sprinkles and MixMe.</td>
</tr>
<tr>
<td>Low quantity LNS</td>
<td>Energy (macro-nutrients) and micronutrients</td>
<td>6–24 mo (manufacturer’s recommendation)</td>
<td>18 mo</td>
<td>An example of a low quantity/energy LNS is Nutributter (product brand name). It is a highly fortified, peanut-based paste that contains vitamins and minerals in addition to providing energy. It is usually packaged in individual daily sachets and is to be eaten either directly from the sachet or added to complementary foods. It is the only product in this table that has been shown to improve linear growth in young children.</td>
</tr>
<tr>
<td>Medium quantity LNS</td>
<td>Energy (macro-nutrients) and micronutrients</td>
<td>6–36 mo (manufacturer’s recommendation)</td>
<td>24 mo</td>
<td>An example of a medium quantity/energy LNS is Plumpy’doz (product brand name). It is a highly fortified, peanut-based paste and contains vitamins and minerals in addition to providing energy. It is usually packaged in individual weekly pots. However, it will also be available in the form of daily sachets, which is the preferred form for distribution. It has been used to prevent increases in GAM in young children during periods of food insecurity.</td>
</tr>
</tbody>
</table>

CSB, corn–soy blend; FBF, fortified blended food; FSP, food supplementation product; GAM, global acute malnutrition; MNP, micronutrient powder; RSB, rice–soy blend; WSB, wheat–soy blend.

a. Product shelf-life under ideal storage conditions.
maintaining selective feeding programs [24]. This has recently been complemented by the publication of the Global Nutrition Cluster Decision Tool on prevention and treatment of MAM [27]. However, although these guidelines do cover prevention, their focus is mainly on acute malnutrition as the key criterion for making decisions to start and stop selective feeding programs. As such, they do not reflect the recent advances in the recognition of micronutrient deficiencies and stunting and the development of programs for their prevention and treatment, which prompted the development of additional manuals such as the Operational Guidance.

As described above, the Operational Guidance is not intended to be a stand-alone document, but rather complements and extends these pre-existing guidelines, widening program targets to include anemia and stunting, as well as acute malnutrition. However, considering the above, it can be seen that there is considerable potential for operational confusion between agencies due to the existence of several overlapping guidance documents on selective feeding, each having a slightly different focus. We therefore propose that the next development that is required is the integration of guidance on the use of new and emerging products with the previously established framework for selective feeding programs. Integration would encourage nutrition programs to consider a wider range of intervention options while clarifying decision criteria and standardizing the consideration of contextual factors. Integration may also reduce confusion over implementation of different selective feeding programs. Inclusion of guidance on nutrition programming within chronic and protracted emergency contexts may also be warranted, particularly as this reflects the majority of refugee and many non-refugee settings.

Additional challenges

Additional challenges included identifying an appropriate duration of use for these products, including recommendations for long-term use (since the contexts within which UNHCR operates are often protracted), the potential for breastmilk displacement while using LNS, and how to ensure appropriate infant and young child feeding practices. However, research so far indicates no difference in breastmilk intake in infants given LNS or porridge [35, 36]. Assessing the effectiveness and cost-effectiveness of the various interventions is another important challenge, as in these contexts: the available data on GAM, stunting, and anemia are derived from cross-sectional surveys, as opposed to longitudinal cohorts; it is usually not feasible to have control groups; and other programs that may impact the measured indicators are often implemented in parallel.

Conclusions and recommendations

The Operational Guidance provides guidance on the process of planning, implementing, monitoring, and evaluating FSP interventions to control and prevent micronutrient deficiencies, stunting, and acute malnutrition in vulnerable groups. Although careful consideration of each stage will help to minimize risks affecting the success of the intervention, it will of course not guarantee success. Because of the multidimensional causes of undernutrition, improvement in nutritional status also requires the integration of appropriate programmatic inputs in water, sanitation, and hygiene; health; infant and young child feeding; and other sectors.

A number of challenges and gaps remain, and it is recommended that future work aim to promote harmonization of LNS nomenclature and classification between different organizations; integration of current guidelines for the prevention and management of acute malnutrition, stunting, and micronutrient deficiencies in emergencies, including guidance on chronic emergency and transitional settings; and analysis of the cost-effectiveness of different intervention options and their affordability in different contexts.

Continued assessment of the impact and use of special nutritional products in emergencies is required, including acceptability and adherence, effectiveness, and cost-effectiveness. Future editions of the Operational Guidance will incorporate feedback from the staff of UNHCR and its partners and will reflect the latest technical advances in this rapidly changing field of nutrition.

Authors’ contributions

Sarah Style was involved in the finalization of the Operational Guidance and produced the first draft of the paper. Melody Tondeur led the development of initial versions of the Operational Guidance. Caroline Wilkinson, Allison Oman, Paul Spiegel, Ismail A. R. Kassim, Carlos Grijalva-Eternod, Carmel Dolan, and Andrew Seal all contributed to the development of the Operational Guidance. Andrew Seal revised the manuscript, and all authors contributed to the final version of the paper.

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