

Fish and Fish-Based Products for Nutrition and Health in the First 1000 Days: A Systematic Review of the Evidence from Low and Middle-Income Countries

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ABSTRACT

Fish provide essential nutrients for the critical window of growth and development in the first 1000 d of life and are thus an attractive option for inclusion in nutrition-sensitive and nutrition-specific programming. We conducted a systematic review of the evidence for fish and fish-based products for nutrition and health outcomes during the first 1000 d of life in low- and middle-income countries, searching the peer-reviewed and gray literature from 1999 to 2020. Databases included PubMed, Web of Science, Embase, ProQuest, and the Clinical Trials repository. Our search returned 1135 articles, 39 of which met the inclusion criteria. All studies were dual evaluated for risk of bias. Of the included studies, 18 measured maternal health and nutrition outcomes and 24 measured infant/child outcomes (3 measured both). Our search uncovered 10 impact evaluations, all of which measured consumption of fish or fish-based complementary food products in children aged 6–24 mo. We did not find strong evidence for fish consumption in children improving child growth from the impact evaluations; however, the studies were highly heterogeneous in their design and likely underpowered to detect an effect. Results from observational studies were mixed but provided evidence that adding fish to maternal and child diets is associated with improved nutrition outcomes, such as reducing the risk of anemia and improving vitamin D status. Given the nutrient richness of fish and the fact that production is often more environmentally friendly as compared with other animal source foods, more robust evidence is needed on the role of fish consumption in nutrition interventions to inform policy and programming recommendations in lowand middle-income countries. Adv Nutr 2022;13:2458–2487.

Statement of Significance: This is the first systematic review providing an overview of the current evidence to date on the role that fish and fish-based products play in addressing the burdens of malnutrition in women and children. Whereas evidence is emerging that fish and fish-based products improve health and nutrition outcomes, more trials with robust study designs are needed to clearly elucidate the benefits.

Keywords: fish, aquatic foods, pregnancy, breastfeeding, complementary feeding, maternal diets, IYCF practices

Introduction

The first 1000 d of life (in utero and age \leq 2 y) is the most critical period for cognition, growth, and development [\(1\)](#page-26-0). Nutrient deficiencies in the first 1000 d can lead to serious adverse health and economic consequences later in life, especially for children in low- or middle-income countries $(2).$ $(2).$

Evidence suggests that fish consumed in the first 1000 d first by pregnant and lactating women and then by infants and children during the complementary feeding period (when the child is 6–23 mo old and foods complement

breastmilk)—has the potential to improve nutrition and health outcomes for these vulnerable populations. During the first 1000 d, nutrients such as iron, zinc, calcium, iodine, vitamin B-12, vitamin A, essential fatty acids, and protein, which are often found in fish, are critical for healthy pregnancies and for the optimal growth and development of young children [\(3,](#page-26-2) [4\)](#page-26-3). Fish of all sizes are higher in essential ω -3 fatty acids when compared with other animal source foods (ASFs), and small fish have a higher micronutrient concentration than large fish [\(4\)](#page-26-3), primarily because they are consumed whole. Furthermore, when small fish-based

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products are dried and powdered, the iron, zinc, calcium, and fatty acid concentrations are comparable to commercially produced complementary food supplements, such as smallquantity lipid-based supplements [\(5\)](#page-27-0). Small fish also have a high reproductive rate and, in some places in sub-Saharan Africa, are sometimes not fished to their maximum sustainable yield [\(6\)](#page-27-1). These characteristics make fish, especially small fish, an appropriate component of programs targeting malnutrition. However, a review of the evidence is needed to inform policy makers and other stakeholders regarding the importance of fish and fish-based products for addressing malnutrition.

Prior systematic reviews on fish consumption have largely focused on high-income countries [\(7,](#page-27-2) [8\)](#page-27-3) or ASFs in general [\(9–11\)](#page-27-4). To our knowledge, no studies have systematically reviewed the evidence on how whole fish or fish-based product consumption during the first 1000 d of life affects the nutrition and health of pregnant and lactating women and infants from low- and middle-income countries. In this systematic review, we collate findings on fish and fish-based products and the role that they play in nutrition and health outcomes of pregnant and lactating women and children <2 y of age to better inform future nutrition interventions for women of reproductive age and children in low- and middleincome countries.

Methods

The PRISMA guidelines informed this systematic review [\(12\)](#page-27-5). To assess the available literature investigating fish and fish-based products and their relationship to nutrition and health outcomes in the first 1000 d, a protocol was developed outlining the systematic review aims, search strategy, and eligibility criteria [\(Table 1\)](#page-2-0). We brainstormed specific search terms that encompassed the diverse array of fish and other aquatic foods and terms that cover the first 1000 d (from pregnancy to \leq 2 y of life). This led to the following search terms:

(fish OR seafood OR prawns OR shrimps OR aquatic animals OR fish powder OR fish-based products) AND (complementary feeding OR complementary food OR mothers OR young children OR infants OR pregnan[∗] OR lactat∗) AND (low-income countr[∗] OR middle-income countr[∗] OR developing countr[∗] OR Africa OR South East Asia OR South America OR Pacific Islands).

Given that the term "aquatic foods" is a relatively new term used by researchers and policy makers, we did not include it

Supplemental Results are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at

[https://academic.oup.com/advances/.](https://academic.oup.com/advances/)

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Abbreviations used: ASF, animal source food; CASP, Critical Appraisal Skills Program; CSB, corn–soy blend; HAZ, height-for-age z score; LAZ, length-for-age z score; ROBINS-I, Risk of Bias in Non-Randomized Studies of Interventions; RUSF, ready-to-use supplementary food; RUTF, ready-to-use therapeutic food; WAZ, weight-for-age z score; WHZ, weight-for-height z score.

in our search. However, if found, studies were included on other aquatic foods (e.g., snails).

In July 2019, we reviewed the literature published in the previous 20 y (1999–2019) and updated the search to an additional year in July 2020 (July 2019–July 2020). We included the following databases in our search: PubMed, Web of Science, Embase, and ProQuest, as well as a hand search of the Clinical Trials repository (clinicaltrials.gov). We also hand searched gray literature sources such as the International Food Policy Research Institute's institutional repository. We reviewed the reference lists of systematic or nonsystematic reviews for studies that met our criteria. The titles and abstracts of all search results were independently screened by one author (KAB) and then by another (JS). Studies that met the inclusion and exclusion criteria were retained, and duplicates were removed. Any discrepancies that involved retaining full-text articles were discussed and resolved between the screeners and, when necessary, a third author. Details of the full-text articles regarding study design, population, setting, interventions/exposures, sample size, analysis methods, outcomes measured, and results were extracted in duplicate into a predefined piloted table (Tables 2a–c). Data extraction was conducted by SM and reviewed by at least 1 other author for accuracy.

Critical appraisals were conducted independently by 2 authors (JS and SM). Disagreements in ratings were discussed and revised between the appraisers and a third author when necessary. Studies were rated as having low, medium, or high risk of bias based on the aspects on their study design and how well the methods and findings were reported. Several critical appraisal tools were used due to the range of study designs in this review. The revised Cochrane risk-of-bias tool for randomized trials [\(13\)](#page-27-6) was used for randomized controlled trials to assess the effect of assignment to interventions. As all interventions were food based, questions on concealment of participants and people delivering interventions were not considered (Nos. 2.1 and 2.2). Yet, questions were assessed as related to researcher and/or outcome assessor concealment prior to analysis (Nos. 1.2 and 4.3). The ROBINS-I (Risk of Bias in Non-Randomized Studies of Interventions; 14) was used for nonrandomized controlled trials. Questions from the ROBINS-I tool pertained to confounding, participant selection, intervention classification, deviations from intended interventions, missing data, outcome measurement, and reporting bias (14) . For cohort (15) and case–control (16) studies, the respective Critical Appraisal Skills Program (CASP) checklists were used. The CASP checklists assessed participant recruitment and selection, exposure measurement, confounding, and internal consistency of results. The CASP Cohort Checklist also included questions on subject follow-up [\(15\)](#page-27-8), whereas the CASP Case–Control Checklist included questions regarding treatment of cases and controls as well as treatment effect size and measurement [\(16\)](#page-27-9). The Appraisal Tool for Cross-Sectional Studies [\(17\)](#page-27-10) was used for cross-sectional studies. Questions assessed sample size justification, selection bias, exposure and outcome

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TABLE 1 Inclusion and exclusion criteria to select studies for the systematic review exploring the relationship between fish and fish-based products and nutrition and health outcomes in low- and middle-income countries^{[1](#page-2-1)}

1HAZ, height-for-age z score; LAZ, length-for-age z score; WAZ, weight-for-age z score; WHZ, weight-for-height z score.

measurement, confounders, nonresponse bias, and internal consistency of results [\(17\)](#page-27-10). Given the large breadth and heterogeneity in interventions, exposures, comparators, and outcomes, all included studies were narratively synthesized.

Results

Overview of included studies

The total number of titles and abstracts screened per the inclusion/exclusion criteria was 1148 [\(Figure 1\)](#page-3-0). Fifty-five full texts were ultimately assessed for eligibility, of which 16 were excluded, resulting in the inclusion of 39 studies. The main reasons for exclusion were that the participants were from a high-income country or the study did not measure a nutrition or health outcome. For example, several studies examined the nutrient content of a fish-based product, rather than how the fish-based product affected the nutrient status of a person. Most studies were cross-sectional $(n = 21)$, followed by randomized controlled trials $(n = 10)$, cohort studies ($n = 6$), case–control studies ($n = 1$), and nonrandomized controlled trials $(n = 1)$.

Study details and demographics

The 39 studies were conducted across 16 low- and middleincome countries. The studies can be divided into observational studies ($n = 29$) [\(Table 2\)](#page-4-0) and impact evaluations $(n = 10)$ [\(Table 3\)](#page-16-0). Of the 39 studies, 14 were in Eastern and [Southern Africa \(](#page-27-13)[18–](#page-27-11)[31](#page-27-12)[\), 5 in West and Central Africa \(32–](#page-27-13) 36), 10 in Southeast Asia [\(37–46\)](#page-27-14), 4 in South Asia [\(47–50\)](#page-28-0), and 5 in Latin America and the Caribbean (all of which were in Brazil) [\(51–55\)](#page-28-1). One study included data from 46 lowand middle-income countries [\(56\)](#page-28-2). The study populations in most studies were infants [\(18,](#page-27-11) [20,](#page-27-15) [22–25,](#page-27-16) [27,](#page-27-17) [29,](#page-27-18) [30,](#page-27-19) [33–42,](#page-27-20) [44,](#page-28-3) [47,](#page-28-0) [51–53,](#page-28-1) [56–58\)](#page-28-2), followed by pregnant and/or lactating women [\(19,](#page-27-21) [32,](#page-27-13) [46,](#page-28-4) [48,](#page-28-5) [49,](#page-28-6) [53,](#page-28-7) [55\)](#page-28-8) and mothers of young children [\(19,](#page-27-21) [27–30,](#page-27-17) [33,](#page-27-20) [37,](#page-27-14) [50,](#page-28-9) [51,](#page-28-1) [53\)](#page-28-7). For the 10 impact evaluations, study durations ranged from 2 to 59 mo. Among the 8 longitudinal studies, Pinto et al. [\(54\)](#page-28-10) had the smallest

FIGURE 1 PRISMA flow diagram for the screening and inclusion of publications in this systematic review that investigated the relationship between fish and fish-based products and nutrition and health outcomes in low- and middle-income countries.

sample size $(n = 146)$ and shortest study duration (9 mo) . The largest sample size was >1 million [\(49\)](#page-28-6) and the longest study duration was $5 \text{ y } (51, 53)$ $5 \text{ y } (51, 53)$ $5 \text{ y } (51, 53)$ $5 \text{ y } (51, 53)$. The sample sizes for the 21 cross-sectional studies ranged from 60 participants [\(41\)](#page-28-11) to 130,432 [\(56\)](#page-28-2). Tables [2](#page-4-0) and [3](#page-16-0) give a breakdown of study designs, exposures, and measured outcomes.

Interventions used in impact evaluations

Of the impact evaluations in which fish was given in the complementary feeding period, 1 study provided fish powder alone (31) , 1 used fish added to a corn porridge (26) , 1 used a Weanimix formulation that included fish [\(36\)](#page-27-23), and 2 used WinFood formulations with fish [\(25,](#page-27-24) [44\)](#page-28-3). The Win-Food studies—1 in Cambodia and 1 in Kenya—compared WinFood with fish against corn–soy blends (CSBs). In Cambodia, researchers used 2 formulations of WinFood: both formulations started with a base of traditional rice porridge (*borbor*) and then incorporated either fish and edible spider or fish only, with a vitamin–mineral mix to the fish-only formulation [\(44\)](#page-28-3). In Kenya, 1 WinFood treatment had a base of germinated amaranth and maize with fish and

edible termite, and 1 formulation had a micronutrient premix instead of fish and termite [\(25\)](#page-27-24).

Ready-to-use supplementary foods (RUSFs) are complementary foods designed to prevent malnutrition, whereas ready-to-use therapeutic foods (RUTFs) are designed to treat malnutrition [\(59\)](#page-28-12). The randomized controlled trial that evaluated an RUSF intervention used an RUSF made of soy, mung bean, coconut, multiple-micronutrient premix, icing sugar, maltodextrin, and canola oil mixed with the fish paste, which was piped into a wafer made from rice flour, egg, water, sugar, salt, and coconut with a small amount of vanilla or sesame seed [\(44\)](#page-28-3). A study conducted in Indonesia evaluated the use of an RUSF cookie, with foxtail millet and tuna listed as the only ingredients [\(39\)](#page-28-13).

In the trials that examined the impact of fish-based products on malnourished children, 1 trial investigated use of an RUTF that consisted of rice, soybean, mung bean, canola oil, and small indigenous fish packed into a wafer [\(57\)](#page-28-14), in a similar formulation to the RUSF developed by the same research group [\(44\)](#page-28-3). In a study that recruited children in Nigeria with rickets (a bone malformation often due to prolonged inadequate vitamin D or calcium intakes), ground

TABLE 2 Observational trials included in a systematic review exploring the relationship between fish and fish-based products and nutrition and health outcomes in low- and middle-income TABLE 2 Observational trials included in a systematic review exploring the relationship between fish and fish-based products and nutrition and health outcomes in low- and middle-income
countries¹

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z score: ASF, animal source food; CSB, com-soy blend; HAZ, height-for-age z score; LAZ, length-for-age z score; RCT, randomized controlled trial; RUSF; ready-to-use supplementary food; RUTF, ready-to-use therapeutic food; WAZ, weig -age ä É ' ASF, animal source food; CSB, com-
WHZ, weight-for-height z score. WHZ, weight-for-height z score.

TABLE 3 (Continued) **TABLE 3** (Continued)

catfish meal was compared with powdered limestone as a source of calcium in the children's diets over a 24-wk period $(35).$ $(35).$

Compliance measures included visual approximation [\(26\)](#page-27-22), weight [\(35,](#page-27-31) [40\)](#page-28-18), count [\(44,](#page-28-3) [57,](#page-28-14) [31\)](#page-27-12), and self-reporting [\(25,](#page-27-24) [36,](#page-27-23) [38\)](#page-27-30) of complementary food consumed. One study did not report any compliance measures [\(39\)](#page-28-13).

Fish exposures in observational studies

We grouped fish exposures into direct or indirect fish consumption [\(Table 4\)](#page-21-0). Exposures were considered direct fish consumption in surveys that recorded fish or aquatic food consumption in mothers [\(27–30, 32,](#page-27-17) [48,](#page-28-5) [50,](#page-28-9) [51,](#page-28-1) [53,](#page-28-7) [54\)](#page-28-10) or infants/children [\(22,](#page-27-16) [23,](#page-27-25) [30,](#page-27-19) [47,](#page-28-0) [52,](#page-28-15) [56,](#page-28-2) [31\)](#page-27-12) without other foods. Exposures were defined as indirect fish consumption when a composite measure was used with other foods (e.g., meat, vegetables). Two studies [\(18,](#page-27-11) [41\)](#page-28-11) that assessed the effects of living in fish-farming households were also considered under the indirect fish consumption category. Composite measures included ASF consumption [\(19,](#page-27-21) [24,](#page-27-26) [49,](#page-28-6) [56\)](#page-28-2), dietary patterns [\(20,](#page-27-15) [21,](#page-27-29) [34,](#page-27-28) [42,](#page-28-16) [55\)](#page-28-8), iron-rich food consumption [\(32\)](#page-27-13), ω -3 fatty acid-rich food consumption [\(37\)](#page-27-14), and vitamin D-rich food consumption [\(46\)](#page-28-4).

The most frequent exposure assessed in observational studies was maternal fish consumption $(n = 9)$. Exposure data collection methods included quantitative and qualitative 24-h dietary recalls [\(19–21,](#page-27-21) [23,](#page-27-25) [24,](#page-27-26) [30,](#page-27-19) [36,](#page-27-23) [42,](#page-28-16) [50,](#page-28-9) [56\)](#page-28-2), FFQs [\(34,](#page-27-28) [37,](#page-27-14) [46,](#page-28-4) [48,](#page-28-5) [49,](#page-28-6) [54,](#page-28-10) [55\)](#page-28-8), nonvalidated food questionnaires [\(27,](#page-27-17) [29,](#page-27-18) [45,](#page-28-17) [47\)](#page-28-0), and nonvalidated but pretested questionnaires [\(32\)](#page-27-13). The weakest fish consumption measures were nonvalidated proxy measures such as hair mercury concentrations [\(51,](#page-28-1) [53\)](#page-28-7) and RBC ω -3 fatty acid concentrations [\(28\)](#page-27-27).

Outcome variables

Outcome variables were highly heterogeneous, falling under maternal, neonatal, and infant outcomes, with maternal and infant outcomes categorized into anthropometric, fatty acid, micronutrient, and other health and/or morbidity outcomes [\(Table 4\)](#page-21-0). Three studies assessed maternal anthropometric outcomes, with indicators covering BMI [\(19,](#page-27-21) [30\)](#page-27-19) and MUAC $(19, 21)$ $(19, 21)$ $(19, 21)$, including arm fat and muscle area (21) . Two studies analyzed maternal fatty acid indicators [\(27,](#page-27-17) [54\)](#page-28-10). A range of maternal micronutrient indicators was cited, such as anemia prevalence [\(32,](#page-27-13) [49\)](#page-28-6), iron [\(21,](#page-27-29) [45,](#page-28-17) [49\)](#page-28-6), zinc [\(45\)](#page-28-17), vitamin D [\(28,](#page-27-27) [46\)](#page-28-4), vitamin E [\(45\)](#page-28-17), and vitamin A [\(45\)](#page-28-17). Two studies assessed maternal depression and anxiety—one postpartum [\(50\)](#page-28-9) and the other during pregnancy [\(55\)](#page-28-8). Three studies reported on neonatal outcomes: low birth weight [\(37,](#page-27-14) [48,](#page-28-5) [53\)](#page-28-7), birth length [\(37,](#page-27-14) [53\)](#page-28-7), and head circumference [\(37\)](#page-27-14).

Most articles assessed infant and child outcomes, with the most reported being anthropometric measures. Growth indices included length- or height-for-age *z* score (LAZ or HAZ) [\(22,](#page-27-16) [23,](#page-27-25) [30,](#page-27-19) [34,](#page-27-28) [36,](#page-27-23) [38,](#page-27-30) [41,](#page-28-11) [42,](#page-28-16) [44,](#page-28-3) [51–53,](#page-28-1) [57,](#page-28-14) [31\)](#page-27-12), weightfor-age *z* score (WAZ) [\(22,](#page-27-16) [30,](#page-27-19) [36,](#page-27-23) [38,](#page-27-30) [39,](#page-28-13) [41,](#page-28-11) [42,](#page-28-16) [44,](#page-28-3) 51– 53, [57,](#page-28-14) [31\), and weight-for-height](#page-28-1) *z* score (WHZ) [\(22,](#page-27-16) [30,](#page-27-19) [34,](#page-27-28) [36,](#page-27-23) [38,](#page-27-30) [41,](#page-28-11) [42,](#page-28-16) [44,](#page-28-3) [51–53,](#page-28-1) [57\)](#page-28-14). Anthropometric indices

consisted of MUAC [\(36,](#page-27-23) [38,](#page-27-30) [44,](#page-28-3) [57\)](#page-28-14), length and weight [\(25,](#page-27-24) [26\)](#page-27-22), head circumference [\(25,](#page-27-24) [36,](#page-27-23) [44\)](#page-28-3), and skinfold thickness [\(25,](#page-27-24) [36,](#page-27-23) [44\)](#page-28-3). Six studies examined population-level indicators such as stunting [\(18,](#page-27-11) [20,](#page-27-15) [24,](#page-27-26) [30,](#page-27-19) [42,](#page-28-16) [56,](#page-28-2) [31\)](#page-27-12), wasting [\(18,](#page-27-11) [24\)](#page-27-26), underweight [\(18,](#page-27-11) [24,](#page-27-26) [42\)](#page-28-16), acute malnutrition [\(23\)](#page-27-25), and overweight/obesity prevalence [\(42\)](#page-28-16). Only 2 studies examined body composition outcomes: fat-free mass [\(25,](#page-27-24) [44\)](#page-28-3) and fat mass [\(25\)](#page-27-24). Four articles examined fatty acid concentrations [\(22,](#page-27-16) [27,](#page-27-17) [29,](#page-27-18) [40\)](#page-28-18). Several studies reported iron status [\(36,](#page-27-23) [41,](#page-28-11) [44\)](#page-28-3) and iron-related indicators such as ferritin [\(22,](#page-27-16) [25,](#page-27-24) [36,](#page-27-23) [41,](#page-28-11) [44\)](#page-28-3), transferrin receptors [\(25,](#page-27-24) [36,](#page-27-23) [44\)](#page-28-3), and hemoglobin concentrations and/or anemia [\(25,](#page-27-24) [36,](#page-27-23) [41,](#page-28-11) [49,](#page-28-6) [52\)](#page-28-15). Vitamin A $(36, 41)$ $(36, 41)$ $(36, 41)$, vitamin D $(22, 47)$ $(22, 47)$ $(22, 47)$, selenium (26) , and zinc status [\(22,](#page-27-16) [26,](#page-27-22) [36,](#page-27-23) [39\)](#page-28-13) were less commonly examined. Some studies examined other health and morbidity outcomes in infants, such as TSH concentrations [\(33\)](#page-27-20), motor development [\(29\)](#page-27-18), rickets [\(35\)](#page-27-31), and environmental enteric dysfunction [\(23\)](#page-27-25), as well as fever, cough, and diarrhea [\(26\)](#page-27-22).

Evidence from impact evaluations

Of the trials that assessed the impact of complementary food, RUSF, or RUTF with fish added on infant and child outcomes, all were randomized controlled trials $(n = 9)$ except for Tichelaar et al. [\(22\)](#page-27-16) [\(Table 4\)](#page-21-0). Thus, the Tichelaar et al. study, which is longitudinal, is summarized in the observational studies section. We uncovered 1 impact evaluation that directly measured fish consumption in the form of a 12-g "daily dose" of fish powder given directly to families [\(31\)](#page-27-12). This 2022 study is included in our review as it was discovered as a planned clinical trial in our initial search [\(58\)](#page-28-19) and results from the trial were published during the revision of this article.

Anthropometric outcomes.

Among the 6 studies that measured fish as an intervention to prevent linear growth faltering (stunting), Skau et al. [\(44\)](#page-28-3) hypothesized and found that the fish-based intervention worked as well as a milk-fortified treatment group, and 3 other studies hypothesized that the fish intervention arm would perform better than a control group [\(25,](#page-27-24) [36,](#page-27-23) [31\)](#page-27-12). Only Chipili et al. [\(31\)](#page-27-12) noted that fish powder significantly improved LAZ. Borg et al. [\(38\)](#page-27-30) found no difference in linear growth between the fish-based intervention and an unsupplemented control group. Lin et al. [\(26\)](#page-27-22) hypothesized that the fish intervention (corn porridge fortified with fish powder) would perform less well than the comparator of a peanut/soy-fortified spread; however, the authors did not observe differences in linear growth between the groups of infants.

Our review uncovered 1 trial investigating a fish-based RUTF on the treatment of severe acute malnutrition [\(57\)](#page-28-14). The trial was designed to evaluate the equivalency of fishbased RUTF (NumTrey) to the standard-of-care RUTF (BP-100 biscuit) among children diagnosed with uncomplicated severe acute malnutrition in Cambodia. The authors did not find any significant differences between the groups in terms of weight gain, WHZ, HAZ, or MUAC; children in both

TABLE 4 Evidence gap map of fish consumption and nutrition and health outcomes in the first 1000 d of life from studies included in a systematic review exploring the relationship between
fish and fish-based products and **TABLE 4** Evidence gap map of fish consumption and nutrition and health outcomes in the first 1000 d of life from studies included in a systematic review exploring the relationship between fish and fish-based products and nutrition and health outcomes in low- and middle-income countrie[s1](#page-21-1)

groups improved after 56 d of the intervention. However, the children in the BP-100 group gained more height after 56 d, though they were slightly shorter and smaller at baseline than the children in the NumTrey group [\(57\)](#page-28-14).

Nutrient status and morbidity outcomes.

Three trials conducted in Ghana [\(36\)](#page-27-23), Kenya [\(25\)](#page-27-24), and Cambodia [\(44\)](#page-28-3) investigated the role of fish and fish-based products on iron status or anemia. Findings from all trials suggested an overall deterioration in iron status over time, regardless of the intervention. Specifically, in Kenya, Konyole et al. [\(25\)](#page-27-24) found that, compared with the CSB groups, both WinFood arms of the study had a decrease in hemoglobin, and the WinFood classic group with fish added had a slightly higher anemia prevalence than the CSB group. Similar findings were reported by Skau et al. [\(44\)](#page-28-3) from a study in Cambodia, in which iron status deteriorated over the intervention period in both WinFood groups (both had ASFs added) and the CSB groups. Research conducted in Ghana by Lartey et al. [\(36\)](#page-27-23) revealed no statistically significant difference in iron status among the 4 types of complementary food, only 1 of which contained fish, but again iron status deteriorated over the 6 mo.

Six studies measured the status of other minerals and vitamins, such as zinc, riboflavin, selenium, calcium, vitamin A, and vitamin D. We uncovered 3 trials that investigated the impact of fish and fish-based products on zinc status [\(26,](#page-27-22) [36,](#page-27-23) [39\)](#page-28-13). Two did not find any evidence of an improvement in zinc status [\(26,](#page-27-22) [36\)](#page-27-23). Yet, a trial conducted in Indonesia found that providing millet biscuit fortified with tuna did improve the zinc status of children aged 6–24 mo [\(39\)](#page-28-13). Also, we did not find evidence of an improvement in selenium [\(26\)](#page-27-22), riboflavin, or vitamin A status [\(36\)](#page-27-23). In a study in Nigeria of children with rickets, 2 treatment groups (ground catfish meal compared with powdered limestone) experienced increases in BMD, calcium, and vitamin D status [\(35\)](#page-27-31). Nurhasan et al. [\(40\)](#page-28-18) looked at the same cohort in Cambodia as Skau et al. [\(44\)](#page-28-3) to investigate serum ω -3 fatty acids in groups given WinFood with small fish added and the CSB groups and did not find any differences.

In addition to assessing nutrition outcomes, 2 trials included morbidity outcomes (prevalence of fever, cough, diarrhea, and respiratory infections) as secondary outcomes [\(26,](#page-27-22) [36\)](#page-27-23). Neither trial found significant differences with respect to morbidity outcomes in children fed fish or nonfish foods.

Evidence from observational studies: Direct fish consumption

Infant and child fish consumption.

Our review uncovered 1 observational trial (case–control) that provided fish directly to children experiencing malnutrition [\(22\)](#page-27-16). The trial was done in South Africa and provided families of undernourished children with catfish fillets 3 times per week for 1 y. The weight and length gain of the undernourished children was compared with a control group of well-nourished children who were not given catfish;

children in the undernourished group gained height and weight faster than the well-nourished control. The catfishsupplemented group also had a higher concentration of DHA and iron than healthy controls after 12 mo, but zinc status deteriorated among the supplemented group [\(22\)](#page-27-16).

Direct fish consumption was measured in nonmalnourished infants and young children in 5 observational studies [\(Table 4\)](#page-21-0), and most provided positive evidence for fish consumption during infancy and early childhood and for nutrition and health outcomes. Out of the 5 studies, 3 examined amount of fish consumed [\(23,](#page-27-25) [30,](#page-27-19) [52\)](#page-28-15) and 2 analyzed the frequency or prevalence of consumption [\(47,](#page-28-0) [56\)](#page-28-2). Four studies were cross-sectional [\(23,](#page-27-25) [30,](#page-27-19) [52,](#page-28-15) [56\)](#page-28-2) and 1 was case–control [\(47\)](#page-28-0). Results were mixed. Three studies showed positive associations with HAZ in certain age groups [\(30,](#page-27-19) [56\)](#page-28-2). In a study in Malawi, children aged 12–36 mo consuming ASFs (mainly made up of fish) had a higher HAZ [\(23\)](#page-27-25). In Zambia, Marinda et al. [\(30\)](#page-27-19) revealed a significant correlation between the quantity of fish consumed by infants aged 6–23 mo and stunting but not between infant fish intake and WHZ. However, Marinda et al. noted a negative association between fish consumption and HAZ in children \geq 24 mo. In a study of 46 low- and middle-income countries, Headey et al. [\(56\)](#page-28-2) cited an association between fish consumption and a reduced prevalence of stunting. On the contrary, Marques et al. [\(52\)](#page-28-15) reported that Brazilian children living in a traditional fishing community had a lower HAZ score when compared with children living in tin-mining communities that consumed less fish. Yet, when Marques et al. investigated associations within groups rather than between, they found that hemoglobin concentrations were correlated to fish consumption only in children in traditional high fish-consuming communities (i.e., they did not find this relationship in the tin-mining community). The case– control study focused on fish consumption in infants and young children and the association with vitamin D status and showed that infants aged 12–24 mo in Bangladesh who did not consume fish were more likely to be vitamin D deficient $(47).$ $(47).$

Maternal fish consumption.

Direct fish consumption among mothers, whether measured by frequency or in quantitative amounts, was measured in 11 observational studies, the highest number of all the exposures. However, 3 studies were reported from the same population in the Amazon basin in Brazil [\(51–53\)](#page-28-1), and another 3 studies were from 1 trial conducted among tribal groups in Tanzania $(27-29)$. All but 2 studies $(30, 54)$ $(30, 54)$ $(30, 54)$ relied on the frequency of fish consumption rather than the quantity.

Findings were mixed on the benefits of maternal fish consumption on maternal outcomes from the 7 studies that investigated this relationship. Multiple studies found an association between maternal fish intake during pregnancy and fatty acid concentrations [\(27,](#page-27-17) [54\)](#page-28-10) and vitamin D concentrations [\(28\)](#page-27-27). Stuetz et al. [\(45\)](#page-28-17) reported a positive association between daily fish paste consumption and iron and vitamin

A status but a negative association with vitamin E among pregnant women in Thailand. Findings from Sparling et al. [\(50\)](#page-28-9) in Bangladesh showed a correlation between fish consumption and mental health, with peripartum women who ate fish on the previous day having lower odds of depression. In urban Zambia, no correlation was revealed between fish consumption and women's BMI [\(30\)](#page-27-19). A trial in Ghana cited no association between consuming fish/snail and anemia among pregnant women, after adjusting for confounding factors [\(32\)](#page-27-13).

From the 5 studies examining maternal fish consumption and its association with neonatal outcomes, findings were again heterogeneous. Muthayya et al. [\(48\)](#page-28-5) indicated that women in India who did not eat fish during the third trimester had a significantly higher risk of delivering a baby with a low birth weight. Yet, evidence from Marques et al. [\(53\)](#page-28-7) suggested that neither birth length nor birth weight differed by frequency of fish consumption among women in Brazil, and no association was noted with HAZ, WAZ, or WHZ when the children were followed up for 5 y [\(53\)](#page-28-7). Cunha et al. [\(51\)](#page-28-1), researching a similar population, also found that the frequency of fish consumption was not associated with HAZ, WAZ, or WHZ in children at 6, 24, and 59 mo. A study in Tanzania did find that maternal fish consumption led to increased infant fatty acid concentrations at 3 mo postpartum but did not report if this then led to improved cognitive development in those infants [\(27\)](#page-27-17). A cross-sectional study based on the same data assessed the association of maternal fish consumption on infant motor development and revealed that increased concentrations of DHA led to a significant increase in observed movement patterns (a measure of infant neurodevelopment) in 3-mo-old infants as compared with infants who had lower DHA in their RBCs [\(29\)](#page-27-18).

Evidence from observational studies: Indirect fish consumption

ASF consumption.

Two studies examined the association of ASF consumption (including fish) with maternal outcomes [\(Table 4\)](#page-21-0). The first was a cross-sectional study in Ethiopia that identified no association between ASF consumption by women and the MUAC or BMI of women of reproductive age [\(19\)](#page-27-21). The second, a large panel survey, found that weekly consumption of fish or meat by women was associated with a 1% increase in hemoglobin concentrations among pregnant women [\(49\)](#page-28-6).

Three studies examined the correlation between fish/meat consumption in women or children and infant outcomes [\(Table 4\)](#page-21-0). Findings by Khamis et al. [\(24\)](#page-27-26) demonstrated that in Tanzania, children aged 6–23 mo who did not consume any fish/meat had a higher likelihood of becoming stunted. However, in terms of wasting and underweight, no significant difference was seen between children who did and did not consume fish/meat [\(24\)](#page-27-26). Nguyen et al. [\(49\)](#page-28-6) found that mothers' fish/meat consumption accounted for a 3% increase in hemoglobin in their children. With respect to morbidity outcomes, Kaimila et al. [\(23\)](#page-27-25) in Malawi did not find a significant association between children's ASF consumption

and acute malnutrition or environmental enteric dysfunction in Malawi.

Dietary patterns.

Three studies assessed whether overall dietary patterns (not just ASFs) that included fish were associated with maternal outcomes [\(Table 4\)](#page-21-0) [\(21,](#page-27-29) [46,](#page-28-4) [55\)](#page-28-8). Thomas [\(21\)](#page-27-29) analyzed associations with anthropometric indicators among HIVinfected pregnant women in Malawi based on different dietary patterns. Pregnant women who consumed a dietary pattern with high fish, meat, and oil showed no difference in MUAC when compared with women who had nonfish dietary patterns. Yet, pregnant women who had the fishbased dietary pattern had significantly lower mean arm muscle area and higher arm fat area than those who consumed a high-grain dietary pattern. Findings from Thomas also indicated that pregnant women who had a dietary pattern based on high fish, meat, and oil had higher hemoglobin concentrations than those with nonfish dietary patterns. A study in Malaysia demonstrated that a dietary pattern that included fish was protective against pregnant women developing a vitamin D deficiency [\(46\)](#page-28-4). Fish-based dietary patterns among pregnant women may be linked to mental health outcomes. In a study by Vilela et al. [\(55\)](#page-28-8), pregnant women in Brazil who consumed a dietary pattern based on fish, vegetable, fruit, and tea had lower anxiety during pregnancy as compared with a dietary pattern based on rice, bean, meat, and egg or bread, sugar, fat, fast food, and snack.

In a cross-sectional study, Angkasa et al. [\(37\)](#page-27-14) assessed the relationship between maternal dietary intake of ω -3 fatty acids (including but not limited to fish) and neonatal outcomes in Indonesia and reported varying results for birth weight based on the type of fatty acid. Although maternal ALA intake was significantly associated with birth weight, DHA and EPA intakes were not. No significant associations were reported for the relationship between intakes of ω -3 fatty acids and birth length/head circumference [\(37\)](#page-27-14).

Four cross-sectional studies [\(20,](#page-27-15) [33,](#page-27-20) [34,](#page-27-28) [42\)](#page-28-16) evaluated the impact of either mother or child dietary patterns (including but not limited to fish) on infant/child outcomes [\(Table 4\)](#page-21-0). No link was identified between maternal seafood consumption and infant TSH concentrations [\(33\)](#page-27-20). In Burkina Faso, Mank et al. [\(34\)](#page-27-28) reported a significant correlation between fishand maize-based dietary patterns in infants aged 8–59 mo on WHZ but not HAZ. Likewise, Melaku et al. [\(20\)](#page-27-15) reported no significant association between stunting in infants/children aged 6–59 mo and a household, maternal, or child dietary pattern of fish and meat. Curiously, findings from Shariff et al. [\(42\)](#page-28-16) in Malaysia suggested that higher consumption of fish, meat, and legumes among children 1–10 y old was linked with higher rates of stunting; however, the researchers did not find this link with underweight, thinness, or overweight/obesity.

Residing in fish-farming households.

Two cross-sectional studies [\(18,](#page-27-11) [41\)](#page-28-11) analyzed the impact of residing in fish-farming households on nutrition outcomes

[\(Table 4\)](#page-21-0). Although findings from Aiga et al. [\(18\)](#page-27-11) in Malawi showed a significant difference in the prevalence of underweight in children between fish-farming and non– fish-farming households, findings from Schipani et al. [\(41\)](#page-28-11) in Thailand suggested no significant differences in *z* scores or micronutrient status (hemoglobin, iron, and vitamin A concentrations) in infants/children.

Risk of bias

A summary of the risk of bias of each study is presented in the online **Supplemental Results**. The ranking of each study (low, medium, and high risk of bias) is presented in [Table 2](#page-4-0) for the observational trials and [Table 3](#page-16-0) for the impact evaluations.

Discussion

Our systematic review investigating the relationship between fish and fish-based product consumption and nutrition/health outcomes revealed a sparse evidence base, showing a slightly positive but still inconclusive association. Reviews of other ASFs have been unable to draw conclusions given the heterogeneity of results [\(9,](#page-27-4) [10,](#page-27-32) [60\)](#page-28-21). Overall, we found *1*) strong evidence that fish intake improves weight gain in malnourished children, *2*) medium-strength evidence that fish intake improves maternal nutrient status, and *3*) emerging evidence that fish intake improves child growth [\(Figure 2\)](#page-25-0).

We did not find any studies that measured child development as an outcome in any time point in the first 1000 d, highlighting an important research gap.

We uncovered 18 observational studies in pregnant and lactating women, 12 of which found a positive relationship with at least 1 maternal, infant, or child nutrition or health outcome. We also uncovered 10 impact evaluations, all of which focused on outcomes in infants and children. Among all the types of studies done in infants and children, 15 of 23 showed a positive relationship between fish consumption and at least 1 nutrition or health outcome. Most observational studies were cross-sectional, so in many cases, the direction of causality is unclear. Increasing fish consumption in lowand middle-income countries holds promise for improving nutrition and health outcomes, but more robust research is needed.

In accordance with other reviews of ASFs [\(10\)](#page-27-32) and nutrition-sensitive agriculture programs [\(61\)](#page-28-22), we found little evidence that interventions using fish or fish-based products had an impact on stunting. However, in trials conducted in 46 low- and middle-income countries and Zambia, Headey et al. [\(56\)](#page-28-2) and Marinda et al. [\(30\)](#page-27-19) respectively showed a positive association between fish consumption and linear growth in children 6–24 mo old. In addition, a trial that published results in 2020 indicated that the daily provision of 12 g of fish powder improved LAZ [\(31\)](#page-27-12). Marinda et al. also demonstrated the importance of disaggregating children by age group to closely examine when fortification of diet with ASF is likely to have the greatest impact, given that the positive association between fish consumption and linear

growth was observed in children aged 6–23 mo and not 24–59 mo. These findings emphasize the importance of intervening at the start of the complementary feeding period for improved child growth.

Stunting, as measured by LAZ or HAZ (for those <2 y and >2 y, respectively), is a difficult indicator on which to detect improvements, often requiring large sample sizes in addition to a robust trial design. Given the resourceintensive nature of randomized trials, we speculate that many impact evaluations in this review were underpowered. Sample sizes in the impact evaluations ranged from \sim 25 to 100 children per treatment arm, but in general, larger sample sizes are needed to detect an effect on linear growth in children [\(62\)](#page-28-23). Nutrition-sensitive agriculture interventions often are based around a theory of change that concludes with improved nutrition and health outcomes, but linear growth is a complex biological phenomenon that has proven difficult to investigate [\(61\)](#page-28-22). Furthermore, stunting is not always the most appropriate indicator to measure in an intervention, and nutrition-sensitive interventions are better suited to measure impacts on diet and household income [\(63\)](#page-28-24).

A similar lack of effect was uncovered for impact evaluations investigating micronutrient status and anemia in children. None of the fish-based interventions improved iron or hemoglobin. In fact, all the children in the studies experienced a decline in iron status over time, which may be due to nondietary factors such as chronic inflammation resulting in poor iron absorption [\(64\)](#page-28-25) or untreated malaria infections [\(65\)](#page-28-26). Additionally, genetics [\(66\)](#page-28-27) and malaria infections [\(67\)](#page-28-28) play a role in iron status, yet these factors were not measured in any of the trials in our review. One study in Indonesia did see an improvement in zinc status by giving children a tuna-fortified biscuit, but this study was classified as having a high risk of bias [\(39\)](#page-28-13).

Additionally, none of the studies on infants and children measured cognitive outcomes, which is an important gap to note, considering that fish are generally a good source of nutrients, such as ω -3 fatty acids, which are important for cognitive development [\(5,](#page-27-0) [68,](#page-28-29) [69\)](#page-28-30). Maternal seafood consumption has been shown to be associated with neurocognitive outcomes in children, but this finding has yet to be replicated in low- and middle-income countries [\(8\)](#page-27-3). There are several trials showing that fish consumption improves the ω -3 fatty acid content of breastmilk [\(68](#page-28-29)[–70\)](#page-28-31), but it is unclear whether maternal fish consumption increases the ω -3 fatty acid concentration enough to influence cognitive development. Because children in low- and middle-income countries face many challenges that negatively influence cognitive development, it is urgent to investigate all resources that could mitigate these challenges [\(71\)](#page-28-32).

There were only 2 impact evaluations: one in Nigeria with catfish meal [\(35\)](#page-27-31) and another in Cambodia with an RUTF made with a small indigenous fish species that included malnourished children [\(57\)](#page-28-14). The study done in Nigeria demonstrated that catfish meal provides a feasible solution for addressing calcium and vitamin D deficiencies in malnourished children [\(35\)](#page-27-31). In Cambodia, using a small

Nutrition and health outcomes from eating fish and other aquatic foods in the first 1000 days - evidence from low and middle income countries

FIGURE 2 Research outcomes ranked by the strength of their evidence in the systematic review investigating the relationship between fish and fish-based products and health and nutrition outcomes in low- and middle-income countries. Available evidence and the strength of the evidence were considered. The strength of evidence was determined by critical appraisals conducted by 2 independent researchers using predefined rubrics specific to the study design, while considering the robustness of the study design.

indigenous fish in an RUSF was as effective in promoting child growth among malnourished children as a milk-based RUSF [\(57\)](#page-28-14). This is promising given that small indigenous fish species are a more acceptable and locally available ASF than milk in certain parts of Southeast Asia [\(43\)](#page-28-20). A longitudinal study that provided catfish fillet to families of malnourished children in South Africa showed an improvement in growth [\(22\)](#page-27-16). However, the children were compared with wellnourished children; therefore, it is unclear if the improvements seen were a result of the catfish fillet improving growth or the children were already headed toward recovery from a malnourished state.

When evaluating the lack of impact of fish and fish-based interventions on nutrition outcomes, one must consider the food matrix within which the fish is delivered. Many fish-based interventions mixed fish powder with a highphytate food, such as maize. Phytates bind to iron and zinc and reduce the availability of these minerals to be absorbed in the gastrointestinal tract [\(72\)](#page-29-0). Although fish is said to have an "enhancing factor" that increases the bioavailability of iron from other foods consumed with the fish [\(73\)](#page-29-1), it is not known if this factor can overcome the antinutrient activity of a high-phytate meal. Although fish powder is considered nutrient dense, interventions in which fish powder was mixed with high-phytate foods likely dampened the effect on micronutrient uptake [\(5\)](#page-27-0). Additionally, the amount of fish used in the interventions might have been too small to affect health and nutrition outcomes, especially with an outcome such as child growth, which is influenced by many factors, including chronic infections [\(74\)](#page-29-2). Indeed, a recent review of ASFs on child growth excluded many fish interventions from the analysis because the amount of fish added to the complementary food in the intervention did not meet the minimum threshold for inclusion [\(9\)](#page-27-4). This highlights the importance of ensuring that the portion sizes of ASF-based interventions, including fish, are given in sufficient amounts to meet the recommended nutrient intakes for the target population.

The evidence for maternal consumption of fish and the correlation with improved status of maternal hemoglobin, ω -3 fatty acids, iron, and vitamin D are encouraging and support the recommendation that fish consumption in pregnant women should be prioritized, supporting findings from other studies in high–fish-consuming communities in high-income countries [\(75\)](#page-29-3). However, aside from Marinda et al. [\(30\)](#page-27-19), all the studies on maternal fish consumption were medium to high risk of bias. Additionally, most of these studies relied on the frequency of fish consumption rather than the quantity consumed. More robust studies are needed that measure the precise amounts of fish consumed to detect an association with maternal and child outcomes.

Fish provided to families must be safe, and although food safety was outside the scope of this review, contaminants

are a concern, as with all perishable foods. Contaminants are often high in fish, and the mercury concentration is so high in fish in the Amazon basin that mercury was used as a marker of fish consumption in the studies conducted in the Latin American region [\(51,](#page-28-1) [53\)](#page-28-7). However, a study from the Seychelles that was not in our review reported no adverse association between maternal mercury intake from fish and neurocognitive outcomes in children, and it found that high maternal DHA intake remained important, even if the fish contained mercury [\(76\)](#page-29-4). In other regions, fish drying and smoking may lead to harmful contaminants such as aflatoxin [\(77\)](#page-29-5) and polycyclic aromatic hydrocarbons [\(78\)](#page-29-6). Thus, food safety remains an important consideration when developing fish-based interventions and programming, and supply chain interventions to improve fish products are needed.

Limitations

Limitations of this study include that it was not preregistered on any platform; regardless, the only change that we made in the methods over the course of the study was to expand the search into the year 2020. Additionally, we included articles written only in English, which may bias the results toward English-speaking countries.

Conclusion

Our findings add to the global discourse that food- and agriculture-based interventions should go beyond targeting 1 outcome (i.e., stunting or anemia reduction) and focus on improving dietary quality through sustainable, nutritionsensitive food systems [\(61\)](#page-28-22). This is so for interventions targeting the critical 1000-d window, as well as interventions targeting households and people outside the 1000-d window more broadly. Although attention is shifting to improving food systems overall, much of the robust research done on the first 1000 d has been on manufactured products—for example, an LNS (lipid-based nutrient supplement) and a micronutrient powder that are shelf stable and designed to provide nutrients in amounts that children aged 6–24 mo need. These products have been justifiably extensively researched through robust randomized trials as well as metaanalyses [\(79–81\)](#page-29-7). Most recently, a meta-analysis based on individual data (rather than study-level data) was done to examine the impact of LNS on health and nutrition outcomes, with favorable results [\(82\)](#page-29-8). However, solutions that are more likely to be available in local settings, such as fish and other ASFs, have not been well researched, and this needs urgent redressing. These solutions are especially relevant for rural settings, given that solutions such as largescale food fortification sometimes do not meet the nutrient requirements of the rural poor, as it does not often purchase or consume enough of the fortified foods [\(83\)](#page-29-9). There has been some robust research on how the provision of ASF can improve outcomes in the first 1000 d, such as evaluations of programs providing livestock [\(84\)](#page-29-10) or eggs to families [\(85,](#page-29-11) [86\)](#page-29-12), but more is needed.

Regardless, fish and the broader category of aquatic foods are gaining recognition in global discourse. An article under

the Blue Foods Assessment project was recently released that published the nutritional values of >3000 aquatic food species and outlined their importance to food and nutrition security [\(87\)](#page-29-13). The current enthusiasm for the potential of fish and other aquatic foods to address malnutrition adds to the urgency of the need for more robust studies. Future studies can design interventions by using locally available foods (e.g., dried small fish) provided to pregnant and lactating women and children aged 6–23 mo and by measuring cognitive development outcomes as well as nutrition outcomes. These studies can also be extended outside the 1000-d window to school-aged children, when the impacts of improved cognitive development are more likely to be detected. In designing new studies, attention should be paid to the role of phytates, which limit iron and zinc absorption. Furthermore, studies of homestead food production with small fish through integrated aquaculture have not been rigorously evaluated for their impact on nutrition and health outcomes, despite analyses providing evidence that interventions such as these are more costeffective than other vitamin A programs (88) .

The environmental and nutritional characteristics of fish and other aquatic foods mean that they have a high potential for addressing the burdens of malnutrition in the first 1000 d, but to date this has not been demonstrated clearly in the scientific research. Food systems that leverage aquatic foods have the potential to improve dietary quality with a relatively low environmental impact, and policy makers need much clearer evidence from researchers on the potential benefits of using these foods to address malnutrition. More attention is needed in this area so that stakeholders can have a clear idea of who will benefit and how much, when investing in fish and fish-based products to address malnutrition and improve the nutrition and health of mothers and children in developing countries.

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