UNIVERSIDADE FEDERAL DO CEARÁ
FACULDADE DE MEDICINA - CAMPUS SOBRAL
PROGRAMA DE PÓS-GRADUAÇÃO EM SAÚDE DA FAMÍLIA

FRANCISCA MAYARA BRASILEIRO GOMES

TRATAMENTO DA ANEMIA FERROPRIVA COM MEDIDAS NÃO FARMACOLÓGICAS: REVISÃO SISTEMÁTICA E META-ANÁLISE

SOBRAL
2022

FRANCISCA MAYARA BRASILEIRO GOMES

TRATAMENTO DA ANEMIA FERROPRIVA COM MEDIDAS NÃO FARMACOLÓGICAS: REVISÃO SISTEMÁTICA E META-ANÁLISE

Dissertação apresentada ao Programa de Pós-graduação *Strictu sensu*, da Universidade Federal do Ceará – UFC, Campus Sobral-CE, como requisito parcial para obtenção do título de Mestre em Saúde da Família.

Orientador: Prof. Dr. Francisco Plácido Nogueira Arcanjo

Sobral

2022

Dados Internacionais de Catalogação na Publicação
Universidade Federal do Ceará
Biblioteca Universitária
Gerada automaticamente pelo módulo Catalog, mediante os dados fornecidos pelo(a) autor(a)

G1t GOMES, FRANCISCA MAYARA BRASILEIRO.
TRATAMENTO DA ANEMIA FERROPRIVA COM MEDIDAS NÃO FARMACOLÓGICAS : REVISÃO SISTEMÁTICA E META-ANÁLISE / FRANCISCA MAYARA BRASILEIRO GOMES. – 2022.
74 f. : il. color.

Dissertação (mestrado) – Universidade Federal do Ceará, Campus de Sobral, Programa de Pós-Graduação em Saúde da Família, Sobral, 2022.
Orientação: Prof. Dr. Francisco Plácido Nogueira Arcanjo.

1. Revisão sistemática. 2. Metanálise. 3. Educação alimentar e nutricional. 4. Anemia ferropriva. 5. Ferro na dieta. I. Título.

CDD 610

FANCISCA MAYARA BRASILEIRO GOMES

TRATAMENTO DA ANEMIA FERROPRIVA COM MEDIDAS NÃO FARMACOLÓGICAS: REVISÃO SISTEMÁTICA E META-ANÁLISE

Dissertação apresentada ao Programa de Pós-graduação *Strictu sensu*, da Universidade Federal do Ceará – UFC, Campus Sobral-CE, como requisito para obtenção do título de Mestre em Saúde da Família.

Aprovada em: 08/07/2022.

BANCA EXAMINADORA

_____

Prof. Dr. Francisco Plácido Nogueira Arcanjo (Orientador)
Universidade Federal do Ceará (UFC)

_____

Profa. Dra. Lissiana Magna Vasconcelos Aguiar (1ª Examinadora)
Universidade Federal do Ceará (UFC)

_____

Prof. Dr. Filipe Nobre Chaves (2º Examinador)
Universidade Federal do Ceará (UFC)

Em memória de Maria Ferreira Gomes e Maria do Socorro Gomes Pinto Siqueira. Aquilo que amamos sempre será parte de nós.

AGRADECIMENTOS

Primeiramente a Deus, por ser essencial em minha vida, Autor de meu destino, meu Guia, Socorro presente na hora da angústia.

À minha família, por sua capacidade de acreditar e investir em mim. Mãe, seu cuidado e dedicação foi que deram, em alguns momentos, a esperança para seguir. Pai, sua presença significou segurança e certeza de que não estou sozinha nessa caminhada. Irmã, por seu apoio, mesmo que indiretamente, e por ser exemplo e inspiração de força e vitória.

Ao meu esposo, obrigada pelo carinho, a paciência e por sua capacidade de me trazer paz e tranquilidade frente a correria da vida. Meu companheiro de vida, presente de Deus.

Aos meus colegas e amigos do mestrado, pelas alegrias, tristezas e dores compartilhadas. Com vocês, as pausas entre um parágrafo e outro melhorou tudo o que tenho produzido na história da vida.

Ao meu orientador Prof. Dr. Francisco Plácido Nogueira Arcanjo, pelo acolhimento, disponibilidade, dedicação e incentivo para conclusão desse trabalho, e por partilhar comigo a felicidade de desfrutar desta alegria. E a todos os professores do curso, que foram tão importantes na minha vida acadêmica e no desenvolvimento deste processo.

Aos funcionários da secretaria do Programa de Pós-Graduação em Saúde da Família pela atenção e disponibilidade.

A todos aqueles que, de alguma forma, estiveram e estão próximos a mim, fazendo esta vida valer cada vez mais a pena.

Agradeço ao mundo por mudar as coisas, por nunca fazê-las serem da mesma forma, pois assim não teríamos o que pesquisar, o que descobrir e o que fazer.

O correr da vida embrulha tudo, a vida é assim: esquenta e esfria, aperta e daí afrouxa, sossega e depois desinquieta. O que ela quer da gente é coragem. O que Deus quer é ver a gente aprendendo a ser capaz de ficar alegre a mais, no meio da alegria, e inda mais alegre ainda no meio da tristeza! (ROSA, 1994, p. 448).

RESUMO

A anemia é um importante indicador de má nutrição e saúde com grandes consequências para o desenvolvimento socioeconômico. Segundo estimativas da OMS, entre 1993 e 2005, a anemia afetou aproximadamente um quarto da população mundial, o que correspondia então a 1,62 bilhão de pessoas afetadas, a maioria crianças com menos de quatro anos. Dentre as causas de anemia, a deficiência de ferro é a mais comum, representando 50% dos casos. Em países em desenvolvimento como o Brasil, a dieta é essencial para o aparecimento da anemia ferropriva. O objetivo é uma revisão sistemática e meta-análise para avaliar a eficácia de medidas não farmacológicas para o tratamento da anemia ferropriva. Bases de dados utilizadas: MEDLINE (via PubMed), biblioteca Cochrane, SciELO/LILACS e EMBASE até junho de 2021. Identificamos todos os ensaios clínicos randomizados que usaram medidas não farmacológicas para tratar anemia feerropriva, incluindo potes/lingotes de ferro ou uso de alimentos foram incluído. Os desfechos de interesse foram as concentrações de hemoglobina (Hb) e a prevalência de anemia. Um total de 479 estudos foram recuperados das bases de dados, dos quais 4 registros duplicados foram removidos. Após a revisão de todos os títulos e resumos, 23 artigos foram considerados potencialmente relevantes, sendo lidos na íntegra e verificados quanto à elegibilidade. Três artigos preencheram todos os critérios de inclusão. Também realizamos uma busca manual de citações e mais 8 registros foram identificados e verificados quanto à elegibilidade. Onze ensaios clínicos foram incluídos nesta revisão. As estimativas mostraram que o uso de medidas não farmacológicas foi associado a um aumento global estatisticamente significativo da Hb média (DM +0,45 g/dL, IC 95% 0,05 a 0,85, p=0,03). O efeito de medidas não farmacológicas sobre a prevalência de anemia ferropriva foi analisado em apenas 5 ECRs. Os participantes dos grupos de intervenção foram 2,78 vezes menos propensos a sofrer de anemia ferropriva do que os dos grupos de controle, OR=2,78, IC 95% 0,93, 8,29, porém sem significância para o efeito geral (p=0,07). As terapias não farmacológicas têm um efeito positivo no equilíbrio de ferro e podem ser um complemento útil aos programas de prevenção e tratamento da anemia por deficiência de ferro em populações de risco. (Número de registro PROSPERO CRD42021261773).

Palavras-chave: Revisão sistemática. Metanálise. Educação alimentar e nutricional. Anemia ferropriva. Ferro na dieta.

ABSTRACT

Anemia is an important indicator of poor nutrition and health with major consequences for socioeconomic development. According to WHO estimates, between 1993 and 2005, anemia affected approximately a quarter of the world's population, which then corresponded to 1.62 billion people affected, most of them children under the age of four. Among the causes of anemia, iron deficiency is the most common, accounting for 50% of cases. In developing countries such as Brazil, diet is essential for the onset of iron deficiency anemia. The objective is a systematic review and meta-analysis to evaluate the effectiveness of non-pharmacological measures for the treatment of iron-deficiency anemia (IDA). Databases used: MEDLINE (via PubMed), Cochrane library, SciELO/LILACS and EMBASE up to June 2021. We identified all randomized controlled trials (RCTs) that used non-pharmacological measures to treat IDA including iron pots/ingots, or food use were included. The outcomes of interest were hemoglobin (Hb) concentrations and prevalence of anemia. A total of 479 studies were retrieved from the databases, of which 4 duplicate records were removed. After, all titles and abstracts were reviewed, 23 articles were considered potentially relevant, and were read in full and checked for eligibility. Three articles met all inclusion criteria. We also conducted a manual search for citations and a further 8 records were identified and checked for eligibility. Eleven RCTs were included in this review. Estimates showed that the use of non-pharmacological measures was associated with a statistically significant overall increase in mean Hb (MD +0.45 g/dL, 95% CI 0.05 to 0.85, p=0.03). The effect of non-pharmacological measures on the prevalence of IDA was analyzed in only 5 RCTs. Participants in the intervention groups were 2.78 times less likely to suffer from IDA than those in the control groups, OR=2.78, 95% CI 0.93, 8.29, however without significance for the overall effect (p=0.07). Non-pharmacological therapies have a positive effect on iron balance and can a useful adjunct to programs to prevent and treat IDA in at-risk populations. (PROSPERO registration number CRD42021261773).

Keywords: Systematic Review. Meta-Analysis. Food and Nutrition Education. Anemia, Iron-Deficiency. Iron, Dietary.

LISTA DE FIGURAS

LISTA DE TABELAS

LISTA DE ABREVIATURAS E SIGLAS

et al.	e outros
FAO	Food and Agricultural Organization
g	Gramas
g/dL	gramas por decilitro
GRADE	Grades of Recommendation, Assessment, Development, and Evaluation
Hb	Hemoglobina
MeSH	Medical Subject Headings
ml	Mililitro
Nº	Número
p.	Página
OMS	Organização Mundial de Saúde
RS	Revisão Sistemática
RoB	Risk of Bias
WHO	World Health Organization

LISTA DE SÍMBOLOS

%	Percentual

SUMÁRIO

1 INTRODUÇÃO

A deficiência de micronutrientes é um importante problema de saúde pública, especialmente em países em desenvolvimento. De acordo com a Organização Mundial da Saúde (OMS), aproximadamente 2 bilhões de pessoas no mundo sofrem de fome oculta, que é a deficiência subclínica de micronutrientes, sendo os principais a vitamina A, ferro, zinco e iodo (WORLD HEALTH ORGANIZATION, 2014).

Alguns indicadores como a baixa renda familiar *per capita*, baixa escolaridade, principalmente materna, maior número de filhos, elevada densidade de morador por cômodo, precárias condições de acesso a serviços públicos, como saneamento básico e energia elétrica, consumo alimentar inadequado, quanti e qualitativamente; predispõem ao risco de desenvolvimento de doenças carenciais, dentre elas a anemia ferropriva **(**OLIVEIRA *et al*., 2010; MORAIS *et al*., 2014).

Devido a sua elevada prevalência, repercussões sobre o crescimento e desenvolvimento, resistência às infecções e associação com a mortalidade em menores de 2 anos, a deficiência de ferro e a anemia carencial ferropriva são consideradas um dos principais problemas de saúde pública, sendo a deficiência nutricional mais comum em todo o mundo (SANTIS *et al*., 2019).

Segundo estimativa da OMS, a anemia acometia, entre os anos de 1993 e 2005 aproximadamente um quarto da população mundial, sendo a maioria crianças menores de quatro anos. A deficiência de ferro foi a principal causa e doenças como malária, esquistossomose e insuficiência renal crônica contribuiram para seu aumento nesse período (KASSEBAUM *et al*., 2014).

No Brasil, em 2006, a estimativa geral da prevalência da anemia era de 25-30%, sendo o segundo colocado, de acordo com a Organização Panamericana de Saúde, dentre os países da América Latina e Caribe com maior prevalência de anêmicos, ficando atrás apenas do Peru (57%) (SOUZA *et al.*, 2013; SILLA *et al*., 2013; CORONA; DUARTE; LEBRÃO, 2014; BORGES; WELFORT, 2011; Amarante *et al*., 2015; MUJICA-COOPMAN *et al.*, 2015).

De modo geral, a anemia instala-se em consequência de perdas sanguíneas e/ou por deficiência prolongada da ingestão de ferro alimentar, principalmente em períodos de maior demanda, como crianças e adolescentes, que apresentam acentuada velocidade de crescimento, além de gestantes e lactantes (SILVA *et al*., 2015).

O ferro pode ser encontrado em vários alimentos, tanto de origem animal (carnes de todos os tipos, leite e ovos), como vegetal (verduras de coloração verde escura, feijão, soja, entre outros). Entretanto, o que precisa ser evidenciado é a capacidade do organismo em aproveitar o ferro presente nestes alimentos, para exercer as suas mais diversas funções, o que determina a sua biodisponibilidade (LOPES *et al*., 2019).

As dietas são classificadas em três categorias quanto a biodisponibilidade de ferro: baixa, intermediária e alta e a absorção média de ferro heme e não heme é aproximadamente 5, 10 e 15%, respectivamente. Dieta com baixa biodisponibilidade (5-10%): é simples, em geral monótona, baseada em cereais, raízes e tubérculos com negligenciáveis quantidades de carne, peixe ou vitamina C, e contém predominantemente alimentos que inibem a absorção do ferro, como arroz, feijão, milho e farinha de trigo integral. Dieta com biodisponibilidade intermediária (11-18%): é composta principalmente de cereais, raízes e tubérculos, mas inclui alguns alimentos de origem animal e/ou ácido ascórbico. A dieta com alta biodisponibilidade (>19%) é diversificada e contém generosas quantidades de carne, aves, peixe e/ou alimentos ricos em ácido ascórbico (WHO, 1989).

Nessa conjuntura, considera-se que o consumo quantitativo e qualitativo adequado de alimentos fontes dos diversos nutrientes é uma alternativa que possui baixo custo e não produz efeitos indesejáveis. Ressalta-se, porém, que modificações nos hábitos alimentares não são rapidamente alcançadas, tornando-se uma estratégia efetiva a longo prazo (KHOSHNEVISAN *et al.*, 2004).

1.1 Justificativa e Relevância

A anemia é um importante indicador de má nutrição e saúde com grandes consequências para o desenvolvimento socioeconômico. Crianças menores de dois anos de idade com anemia grave têm maior risco de mortalidade e, mesmo as formas leves, que podem ser corrigidas, causam danos cognitivos permanentes como déficit de atenção e memória (MAGALHÃES; CLEMENTS, 2011; CENTRAL STATISTICAL AGENCY ETHIOPIA; ICF INTERNATIONAL, 2012).

A deficiência de ferro, no Brasil, é mais encontrada que outras deficiências, como a hipovitaminose A, a carência primária de iodo e a desnutrição energético-protéica. Entretanto, a

ferropenia também pode advir de perda sanguínea. Nas mulheres em idade fértil, a perda menstrual é a maior causa não nutricional de ferropenia, já nos homens e nas mulheres pós menopausa, o responsável é o sangramento do trato gastrointestinal. É importante não subvalorizar ou banalizar a doença, mesmo quando leve e oligossintomática, haja vista que prejuízos socioeconômicos, intelectuais e de qualidade de vida podem advir deste problema. Isso sem contar o aumento da mortalidade nas populações biologicamente mais frágeis (CANÇADO; CHIATTONE, 2010; WHO, 2011; SILVA; VIEIRA, 2021).

Dentre as causas de anemia, a anemia por deficiência de ferro é a mais comum, responsável por 50% dos casos. Em países em desenvolvimento como o Brasil, a dieta é fundamental no aparecimento da anemia por ferropenia, principalmente porque o ferro, embora esteja presente em cereais e leguminosas (alimentos de mais fácil acesso), está em sua forma de baixa disponibilidade. Portanto, nos grupos de risco é necessário estimular o consumo de ferro de origem animal, em sua forma ativa, a fim de prevenir a causa mais prevalente de anemia (FABIAN *et al.*, 2007; CANÇADO; CHIATTONE, 2010; BORGES; WELFORT, 2011; MUJICA-COOPMAN *et al.*, 2015; LOPEZ *et al.*, 2016; BEZERRA *et al.*, 2018).

Uma vez que, a composição na qualidade e quantidade de ferro consumidos atraves dos alimentos condicionam fatores de risco para o desenvolvimento da ferropenia e anemia ferropriva, levanta-se o seguinte questionamento: Seria possivel tratar a anemia ferropriva ataravés de manejos alimentares ou com outras medidas nao farmacologicas?

Diante disso, a investigação de estudos que buscam alternativas não medicamentosas para o tratamento da anemia mostra extrema relevancia na perspectiva de demonstrar a possibilidade de diminuir a prevalencia de anemia e seus efeitos deletérios em populacões menos favorecidas através do manejo alimentar adequado.

2 OBJETIVOS

2.1 Objetivo Geral

- Realizar uma revisão sistemática sobre alternativas não farmacológicas para o tratamento da anemia, seus efeitos sobre as concentrações de hemoglobina e prevalência de anemia.

2.2 Objetivos Específicos

- Observar nas evidências científicas, o efeito do uso de panela de ferro e lingote de ferro sobre os níveis de hemoglobina e prevalência de anemia;

- Identificar o efeito da alimentação sobre os níveis de hemoglobina e prevalência de anemia.

3 REFERÊNCIAL TEÓRICO

3.1 Anemia ferropriva

A anemia é uma condição patológica em que ocorre diminuição da massa de hemoglobina e da massa eritrocitária (SANTIS *et al.*, 2019). De acordo com a OMS, pode-se classificar a significância populacional da prevalência de anemia como normal ou aceitável (abaixo de 5%), leve (de 5 a 19,9%), moderada (de 20 a 39,9%) e grave (maior ou igual a 40%). Em termos mundiais, a prevalência de anemia em países industrializados é ainda inaceitável, situando-se em torno de 5 a 16%. Estimou-se que, entre os anos de 1990 e 1995, nos países desenvolvidos, a anemia acometeu 20% das crianças menores de cinco anos, 22% das gestantes, 10% das mulheres não grávidas, 4% dos homens e 12% dos idosos. Em contraponto, nos países em desenvolvimento, essas proporções seriam de 39%, 52%, 42%, 30% e 45%, respectivamente, atingindo, portanto, razões de prevalência de até 7,5 e traduzindo sua gravidade nesses locais (WHO, 2001).

Dentre as anemias, destaca-se a anemia ferropriva, que apresenta maior incidência em relação as demais, está caracteriza por privação de ferro dentro do organismo ocasionando uma redução na hemoglobina (LOPES *et al*., 2019). Anemia ferropriva é conhecida como sendo uma das carências nutricionais mais prevalentes no mundo, pois ocorre em consequência de perda sanguínea, pouca ingestão de ferro ou absorção deficiente, perdas urinárias e aumento do volume sanguíneo (AMARANTE *et al*., 2015).

A anemia ferropriva resulta da redução dos níveis de ferro na corrente sanguínea. Os locais de reserva de ferro dos macrófagos estão depletados, dessa forma, não é possível disponibilizá-lo ao plasma. Por consequência, a concentração plasmática de ferro cai a números que suprimem a eritropoiese. Acomete com maior frequência mulheres em idade fértil, lactentes e crianças menores de 5 anos (HASSAN *et al*., 2016).

Entre os fatores relacionados com a anemia ferropriva estão o primeiro trimestre de gravidez, período que ocorre pouco depósito de ferro e oferta insuficiente devido a formação do feto; baixo peso no nascimento, clampeamento precoce do cordão umbilical, pequeno período de aleitamento materno, assim como a introdução tardia da alimentos ricos em ferro na dieta, locais com altitudes elevadas (NAFI; TAZI; MAHMAL, 2015).

Torna-se importante destacar sobre os consensos relacionados aos pontos de corte para a

anemia. Para a OMS, a anemia é definida com concentração de Hb inferior a 12 g/dL para mulheres pré-menopausa e inferior a 13,0 g/dL para homens e mulheres na fase pós-menopausa, ambos os valores considerados para o nível do mar; já na infância, a anemia ocorre quando o nível de hemoglobina no sangue encontra-se abaixo de 11g/dL para menores de seis anos e abaixo de 11,5g/dL para crianças de seis a onze anos de idade (WHO, 2001). Outros autores propõem limite inferior de 13,7 g/dL para homens caucasianos com idade entre 20 e 59 anos e de 13,2 g/dL para aqueles com 60 anos ou mais; e de 12,2 g/dL para mulheres com 20 anos ou mais. Para afrodescendentes adultos, os valores dos limites inferiores recomendados são de 12,9 g/dL (20-59 anos) e de 12,7 g/dL (≥ 60 anos) para homens e de 11,5 g/dL para mulheres com mais de 20 anos (BEUTLER *et al.*, 2006).

3.2 Estratégia não farmacológicas para tratamento da anemia

Existem várias estratégias para prevenir e/ou tratar a deficiência de ferro e a anemia por deficiência de ferro: modificação e diversificação da dieta que visa aumentar o conteúdo e a biodisponibilidade de ferro na dieta (FAO/CAB INTERNATIONAL, 2011); suplementação preventiva ou intermitente de ferro por meio de comprimidos, xaropes ou gotas; transfusão de sangue, indicada apenas para anemia muito grave; biofortificação por meio de melhoramento convencional de plantas ou engenharia genética que aumenta o teor de ferro ou sua biodisponibilidade em plantas e vegetais comestíveis; e fortificação com compostos de ferro de alimentos básicos (normalmente milho, soja e farinha de trigo) no ponto de produção ou moagem (WHO/FAO 2006; WHO 2017).

Ações de educação alimentar e nutricional voltadas para a prevenção da anemia ferropriva preveem o estímulo ao acesso universal à alimentação adequada, ao aleitamento materno exclusivo e prolongado, de forma a aumentar o consumo de alimentos fontes de ferro, bem como de alimentos que aumentam a biodisponibilidade e a absorção do ferro na introdução de alimentos complementares (FISBERG; LYRA; WEFFORT, 2018).

Os alimentos fontes de ferro devem ser recomendados, principalmente as carnes vermelhas, vísceras (fígado e miúdos), carnes de aves, peixes e hortaliças verde-escuras, entre outros. Para melhorar a absorção do ferro, recomenda-se a ingestão de alimentos ricos em vitamina C, disponível nas frutas cítricas, como laranja, acerola e limão, evitando-se excessos de

chá ou café, que dificultam esta absorção (WHO, 2001; SILLA *et al.*, 2013). Uma alternativa como suplemento alimentar de ferro é o mel da cana-de-açúcar que, segundo o Departamento de Agricultura dos Estados Unidos (2016), pode ser usado como um adoçante natural, um substituto nutritivo do açúcar porque é rico em cálcio, ferro, magnésio, selênio e outros nutrientes importantes (Tabela 1).

Tabela 1. Principais vitaminas e composição mineral do mel de cana-de-açúcar (porção de 18,6g).

Niacina	0,173 mg
Vitamina B6	0,125 mg
Cálcio	38 mg
Ferro	0,88 mg
Magnésio	45 mg
Fósforo	6 mg
Potássio	272 mg
Sódio	7 mg
Zinco	0,05 mg

Fonte: Departamento de Agricultura dos Estados Unidos, 2016.

Na América Latina (especialmente no Brasil e Venezuela) e os países do Caribe, um alimento regional que é rico em ferro, prontamente disponível e de baixo custo é a rapadura – um adoçante branqueado não refinado. Rapadura é um suco seco essencialmente puro, obtido da usina de cana-de-açúcar e preparado e distribuído em forma de um bloco (um método originalmente criado para facilitar o seu transporte). Produzido em grande escala na planta de cana-de-açúcar em regiões tropicais, a rapadura é usada como um substituto mais barato e acessível para açúcares refinados. Também é mais saudável do que o açúcar refinado, produto em que o fluxo de açúcar não é separado do melaço, que ajuda a reter a maior parte de seus nutrientes essenciais, vitaminas e minerais (Departamento de Agricultura e Agricultura dos Estados Unidos, 2001).

Entre as várias estratégias que estão sendo investigadas para diminuir a prevalência e a gravidade da anemia por deficiência de ferro é o fornecimento de recipientes para cozinhar feito de liga de fero ou ferro. Em estudos envolvendo crianças menores de 5 anos de idade na Etiópia e no Brasil demonstrou que comer alimentos cozidos em potes de ferro aumentaram a concentração de hemoglobina (BORIGATO; MARTINEZ, 1998; A ADISH *et al.*, 1999).

A contraindicação de uso de leite de vaca in natura, não processado, em pó ou fluido antes

dos 12 meses (limitação de consumo de 500ml/dia após os 12 meses) também é uma estratégia reconhecidamente protetora contra a deficiência de ferro e o desenvolvimento de anemia ferropriva, devendo ser continuamente incentivada. Estilos de vida optantes por regimes de alimentação restritos para o uso de carnes e alimentos fontes de ferro hemínico requerem igualmente acompanhamento nutricional adequado, com apoio de nutricionistas especialistas para garantir o consumo adequado de ferro e ou suplementação profilática sempre que necessário (SOCIEDADE BRASILEIRA DE PEDIATRIA, 2003; BRASIL, 2018).

Os esforços e as estratégias gerais na prevenção da deficiência de ferro devem contemplar a redução da pobreza, o acesso a dietas diversificadas, a melhora nos serviços de saúde e saneamento e a promoção de melhores cuidados com as práticas de alimentação. O tratamento preventivo e sustentável da deficiência de ferro inclui, primordialmente, a garantia do aporte nutricional necessário de ferro para essa população vulnerável (WHO, 2001).

4 MÉTODOS

4.1 Design de estudo

Consiste emu ma revisão sistemática e meta-análise que verificou a eficácia e segurança do uso de medidas não farmacológicas no tratamento da anemia.

4.2 Definição do problema clínico

A definição da questão específica foi realizada sob a sigla PICOT, conforme figura 1.

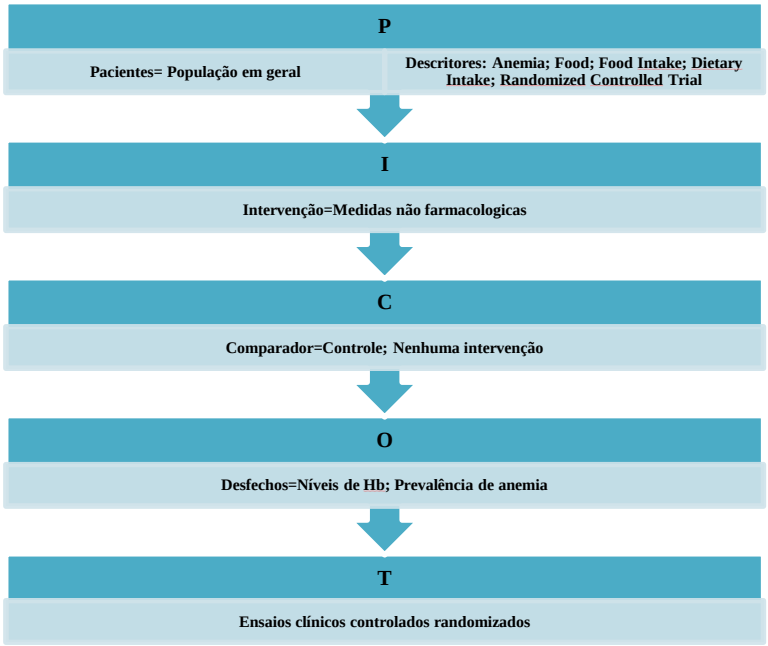


Figura 1. Pergunta PICOT

4.3 Fontes de informação

Para a realização deste estudo, foram utilizadas as bases de dados MEDLINE (via PubMed), biblioteca Cochrane, Scielo/LILACS e EMBASE. Eles foram pesquisados sem restrições de datas ou idiomas. Além disso, a lista de referência dos estudos incluídos também foi analisada manualmente pelos revisores.

Esta revisão foi desenhada e conduzida de acordo com as recomendações PRISMA por

Liberati *et al*. (2009), e o protocolo de pesquisa (ANEXO A) foi registrado no PROSPERO (Material suplementar A), com o número de registro: CRD42021261773.

4.4 Estratégias de pesquisa

Para recuperar os artigos, os seguintes termos de pesquisa foram usados (a última data de pesquisa foi junho de 2021) usando os operadores booleanos OR e AND. Para a base de dados Scielo foi utilizado os operadores (Anemia) AND (Food). Na biblioteca Cochrane os termos descritos foram (Anemia), (Food Intake), (Randomized Controlled Trial) inseridos sem modificação. No entanto, para realizar a busca nas bases de dados MEDLINE (via PubMed) e EMBASE, foram inseridos os termos MeSH e EMTREE, respectivamente.

Portanto, para realizar a pesquisa no PubMed, os termos MeSH apropriados foram pesquisados primeiro. Ao inserir a condição estudada (Anemia) a plataforma gerou os seguintes termos: “Anemia”. Para o termo (Food Intake), foi gerado: (Intake, Food) OR (Nutrient Intake) OR (Intake, Nutrient) OR (Nutrient Intakes) OR (Nutritional Intake) OR (Intake, Nutritional) OR (Nutritional Intakes) OR (Dietary Intake) OR (Dietary Intakes) OR (Intake, Dietary) OR (Micronutrient Intake) OR (Intake, Micronutrient) OR (Micronutrient Intakes) OR (Ingestion) OR (Feed Intake) OR (Feed Intakes) OR (Intake, Feed) OR (Macronutrient Intake) OR (Intake, Macronutrient) OR (Macronutrient Intakes) OR (Calorie Intake) OR (Calorie Intakes) OR (Intake, Calorie) OR "Eating"[Mesh].

Os seguintes filtros para ECRs já padronizados para este tipo de estudo por A Robinson e Dickersin (2002) foram associados aos termos MeSH já descritos: (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh] OR ("clinical trial"[tw]) OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR ("latin square"[tw]) OR placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR follow-up studies[mh] OR prospective studies[mh] OR cross-over studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw]) NOT (animal[mh] NOT human[mh]).

Para pesquisar a plataforma EMBASE, além dos termos listados acima, os termos EMTREE foram usados: 'iron deficiency anemia'/exp AND 'iron deficiency'/exp AND ('food

intake'/exp OR 'appetite regulation' OR 'feed intake' OR 'feeding methods' OR 'food consumption' OR 'food ingestion' OR 'food intake' OR 'food intake regulation' OR 'food uptake' OR 'meal.

Além dessa estratégia de pesquisa, foi realizada uma busca manual nas referências citadas pelos artigos selecionados que eram potencialmente elegíveis e que não foram contemplados pela busca previamente realizada nas bases de dados.

4.5 Seleção dos estudos

Ensaios clínicos controlados randomizados que utilizaram medidas não farmacológicas para o tratamento da anemia por deficiência de ferro, incluindo panelas de ferro, lingotes de ferro, ou uso de alimentos. Não houve restrição da faixa etária. Excluímos estudos que não incluíram dados quantificáveis.

4.6 Extração de dados

Os estudos foram analisados a partir das informações extraídas, expostos por meio do instrumento em forma de tabelas, a fim de imprimir maior clareza dos resultados, sendo organizados com dados sintetizados de cada artigo encontrado, tais como: nome do artigo, autor principal, ano, país, objetivos, número e idade dos participantes, duração da intervenção e desfechos analisados (Tabela 2).

Tabela 2. Síntese dos artigos encontrados.

	Nome do Artigo	Autor Principal/ Ano/ País	Amostra(n)/ Duração da intervenção	Objetivos/Parâmetros analisados
1	Iron Nutritional Status Is Improved in Brazilian Preterm Infants Fed Food Cooked in Iron Pots*.	Borigato 1998 Brasil	45 crianças entre 4 e 12 meses de vida/ 08 meses	Determinar a eficácia do cozimento de alimentos em panelas de ferro para prevenir a anemia em prematuros/ Avaliados valores da Hb, Ht e ferritina sérica.
2	Effect of consumption of food cooked in iron pots on iron status and growth of young children: A randomised	Adish 1999 Etiópia	407 crianças entre 02 e 05 anos de idade/ 12 meses	Avaliar os efeitos do uso de panelas de ferro e alumínio sobre a mudança na concentração da Hb, peso e comprimento das crianças.

	trial*			
3	The effect on haemoglobin of the use of iron cooking pots in rural Malawian households in an area with high malaria prevalence: A randomized trial.	Geerligs 2003 Malaui	41 famílias, totalizando 322 pessoas entre adultos e crianças maiores de 01 ano de idade/ 20 semanas	Avaliar os efeitos do cozimento em panelas de ferro ou alumínio em domicílios de uma área com alta prevalência de malária, sobre status da Hb e prevalência da deficiência de Ferro.
4	Is cooking food in iron pots an appropriate solution for the control of anaemia in developing countries? A randomised clinical trial in Benin.	Sharieff 2007 Benim	339 pessoas entre crianças (6-24meses), adolescentes (11-15 anos) e mulheres (15 a 44 anos) 06 meses	Avaliar o efeito de dois tipos de panelas de ferro sobre as concentrações de Hb e ferritina.
5	Food-based strategies improve iron status in toddlers: a randomized controlled trial*	Szymlek-Gay 2009 Nova Zelândia	225 crianças saudáveis não anêmicas de 12 a 20 meses/ 20 semanas	Determinar a eficácia de um aumento da ingestão de carne vermelha, ou o consumo de leite não fortificado, na melhoria do nível de ferro em crianças em nível populacional.
6	Effect of a beverage fortified with evaporated sugarcane juice on hemoglobin levels in preschool children*	Arcanjo 2009 Brasil	352 crianças de 2 e 3 anos/ 12 semanas	Medir o efeito do consumo de uma bebida misturada com um alto adoçante de ferro (caldo de cana evaporado conhecido como rapadura) nos níveis de hemoglobina em crianças em idade pré-escolar, e compará-lo com o efeito de consumir a mesma bebida doce com açúcar refinado.
7	Evaluation of the effectiveness of stainless steel cooking pots in reducing iron-deficiency anaemia in food aid-dependent populations.	Talley 2009 Tanzania	110 crianças (6-59 meses) e 110 mulheres (suas mães) 12 meses	Avaliar a eficácia de panelas de aço inoxidável (liga de Fe) em redução da anemia por deficiência de Fe em populações dependentes de ajuda alimentar.
8	A Randomized Control Trial Using a Fish-Shaped Iron Ingot for the Amelioration of Iron Deficiency Anemia in Rural Cambodian Women.	Charles 2015 Camboja	248 mulheres/ 12 meses	Determinar se cozinhar alimentos com um lingote de ferro aumenta a hemoglobina e ferritina sérica de mulheres e se as mulheres usariam um lingote de ferro no formato de um peixe.
9	Randomized controlled trial assessing the efficacy of a reusable fish-shaped iron ingot to increase hemoglobin concentration in anemic, rural Cambodian women.	Rappaport 2017 Camboja	326 mulheres de 18 a 49 anos/ 12 meses	Determinar a diferença nas concentrações de hemoglobina em mulheres rurais cambojanas anêmicas que cozinharam com lingote de ferro.

10	Iron Pots for the Prevention and Treatment of Anemia in Preschoolers*	Arcanjo 2018 Brasil	151 crianças entre 04 e 05 anos de idade / 16 semanas	Avaliar o efeito de alimentos cozidos em panelas de ferro e mudança na concentração de Hb e prevalência da anemia.
11	Sugar Cane Honey is as Effective as Weekly Iron Supplementation to Prevent and Treat Anemia in Preschoolers*	Arcanjo 2020 Brasil	176 crianças de 24-36 meses/ 16 semanas	Comparar o efeito do mel de cana-de-açúcar, solução oral de sulfato ferroso e controle sobre concentrações de hemoglobina e prevalência de anemia em pré-escolares.

*Estudos realizados apenas com crianças.
Fonte: Elaborada pela autora.

4.7 Avaliação do risco de viés

O risco de viés nos estudos incluídos foi avaliado usando a ferramenta Cochrane Risk of Bias (RoB 2.0) disponibilizado pelo *Cochrane Review Group Starter Pack* (2020). Essa ferramenta é composta por cinco domínios, os quais são baseados em evidência empírica, mas considerações teóricas também foram levadas em conta para a escolha deles.

Os domínios avaliados na ferramenta RoB 2 são: 1) viés no processo de randomização; 2) viés devido a desvios das intervenções pretendidas; 3) viés devido a dados faltantes dos desfechos; 4) viés na mensuração dos desfechos; e 5) viés na seleção dos resultados relatados. O julgamento dos domínios é classificado em “baixo risco de viés”, “algumas preocupações” e “alto risco de viés” (HIGGINS *et al.*, 2021).

4.8 Síntese dos resultados

Os dados foram resumidos e agregados numa síntese quantitativa por meio de uma meta-análise apresentada usando o gráfico de floresta (ou *forest plot*, em inglês). Usamos o software estatístico Review Manager (2014), fornecido pela Cochrane para analisar os dados. Avaliamos nossos efeitos de intervenção com meta-análises de efeitos aleatórios e efeito randômico e relatar o resultado com análises de dois desfechos, em dois gráficos: 1) Índice de Hb de todos os estudo selecionados, subdividindo em subgrupos de alimento e panela de ferro/lingote de ferro, 2) Prevalência de anemia, subdividindo em subgrupos com alimento e panela de ferro/lingote de ferro; também foram apresentados dados de estudos realizados apenas com crianças com as mesmas subdivisões.

4.9 Avaliação da qualidade da evidência

Foi realizada a avaliação da qualidade usando o Grades of Recommendation, Assessment, Development, and Evaluation (GRADE), garantindo assim um processo sistemático e transparente nesse processo da RS. Esse sistema classifica as evidências em alta, moderada, baixa ou de muito baixa qualidade, levando em conta todos os fatores que determinam o quanto confiável são os resultados (SCHÜNEMANN *et al.*, 2021). Serão avaliados dois desfechos, uma para os estudos que avaliam os índices de Hb (todos os 11 estudos), e outra para aqueles que avaliam além desses valores, a prevalência de anemia (05 estudos).

A qualidade da evidência sempre começa como “alta” (não há preocupações em nenhum dos fatores avaliados), podendo ser rebaixada em até três níveis (chegando à qualidade “muito baixa”), de acordo com a avaliação dos cinco domínios que compõem a avaliação GRADE (GUYATT *et al.*, 2008; GRADE, 2020).

5 RESULTADOS

Os resultados foram apresentados através do artigo "**Non-pharmacological measures for the treatment of iron deficiency anemia: A systematic review and meta-analysis"** disponível para pré-impressão na medRxiv The Preprint Server for Health Sciences.

Non-pharmacological measures for the treatment of iron deficiency anemia: A systematic review and meta-analysis

Short Title: Review of non-pharmacological measures for IDA

Francisca Mayara Brasileiro Gomes[1]; Francisco Plácido Nogueira Arcanjo[1]; Francisco Leandro Fonteles Moreira[2]; Ivana Cristina de Holanda Cunha Barreto[3]; Luiz Odorico Monteiro de Andrade[2,3]; Thiago Corrêa de Oliveira[2,4]; Eliana Pereira Vellozo[5]; Benjamin Israel Kopelman[6]; Cecília Costa Arcanjo Freire[1,2,4]; Caio Plácido Costa Arcanjo[4,7]; Maria Aparecida Zanetti Passos[8].

[1] Postgraduate Program in Family Health, Universidade Federal do Ceará, Sobral, Brazil.

[2] Faculty of Medicine, Universidade Federal do Ceará, Sobral, Brazil.

[3] Researcher at the Osvaldo Cruz Foundation, Ceará, Brazil.

[4] Centro Universitário INTA, Sobral, Ceará, Brazil.

[5] Postdoctoral student in Pediatrics and Sciences Applied to Pediatrics at the Universidade Federal de São Paulo. Outpatient Supervisor of the Adolescent Medicine Sector, Department of Pediatrics, Universidade Federal de São Paulo. Co-advisor of the Postgraduate Program in Pathology at the Universidade Federal de São Paulo.

[6] Advisor of the Graduate Program in Pediatrics and Sciences Applied to Pediatrics at the Universidade Federal de São Paulo, São Paulo, Brazil; Associate Professor, Discipline of Neonatal Pediatrics, Department of Pediatrics, Universidade Federal de São Paulo, São Paulo, Brazil.

[7] Postgraduate Program in Health Sciences, Universidade Federal do Ceará, Sobral,

Brazil.

[8] Postgraduate Program in Education and Health in Childhood and Adolescence, Universidade Federal de São Paulo / Escola Paulista de Medicina, São Paulo, Brazil.

Corresponding author

Francisco Plácido Nogueira Arcanjo, PhD

Postgraduate Program in Family Health Universidade

Federal do Ceará - Campus Sobral

Av. Comandante Maurocélio Rocha Ponte, 100 – Derby

Sobral, Ceará, 62.042-280, Brazil. Telefax:

+55 88 3677 8000

E-mail: franciscoplacidoarcanjo@gmail.com ORCID:

0000-0002-9020-3092

Other authors

Francisca Mayara Brasileiro Gomes, e-mail: mayarabrasileiro09@gmail.com ORCID: 0000-0002-6641-3698

Francisco Leandro Fonteles Moreira, e-mail: fontelesmoreira@gmail.com ORCID: 0000-0002-4380-1217

Ivana Cristina de Holanda Cunha Barreto, e-mail: ivana.barreto@fiocruz.br ORCID: 0000-0001-8447-3654

Luiz Odorico Monteiro de Andrade, e-mail: odorico.monteiro@fiocruz.br ORCID: 0000-0002-3335-0619

Thiago Corrêa de Oliveira, e-mail: tcoliveiraufc@gmail.com

Eliana Pereira Vellozo, e-mail: eliana.vellozo@unifesp.br ORCID: 0000-0002-8928-0699

Benjamin Israel Kopelman, e-mail: b.kopelman@unifesp.br ORCID: 0000-0002-5261-4296

Cecília Costa Arcanjo Freire, e-mail: cecilia_arcanjo@hotmail.com ORCID: 0000-0002-2747-4623

Caio Plácido Costa Arcanjo, e-mail: caioplacidoarcanjo@gmail.com ORCID: 0000-0002-5854-6650

Maria Aparecida Zanetti Passos, e-mail: cidazpassos94@yahoo.com.br ORCID: 0000-

0003-4626-0871

Ethics declarations

Ethical considerations

This review was conducted according to established scientific guidelines. Every attempt has been made to be fair and respectful to the authors discussed.

Conflicts of interest

The authors declare that they have no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Manuscript details

Number of Tables: 2

Number of Tables (online only): 0 Number

of Figures: 7

Word count in abstract: 250

Wordcount in manuscript (excluding tables and figures): 3295 References:

34

Keywords: Iron-deficiency anemia; Hemoglobin concentration; Disease prevention; Complementary therapies; Review.

Abstract

Objective: To conduct a systematic review and meta-analysis to evaluate the effectiveness of non-pharmacological measures for the treatment of iron-deficiency anemia (IDA).

Data sources: MEDLINE (via PubMed), Cochrane library, SciELO/LILACS and EMBASE up to June 2021

Study selection and data extraction: We identified all randomized controlled trials (RCTs) that used non-pharmacological measures to treat IDA including iron pots/ingots, or food use were included. The outcomes of interest were hemoglobin (Hb) concentrations

and prevalence of anemia.

Results: 479 studies were retrieved from the databases, of which 4 duplicate records were removed. After, all titles and abstracts were reviewed, 23 articles were considered potentially relevant, and were read in full and checked for eligibility. Three articles met all inclusion criteria. We also conducted a manual search for citations and a further 8 records were identified and checked for eligibility. Eleven RCTs were included in this review. Estimates showed that the use of non-pharmacological measures was associated with a statistically significant overall increase in mean Hb (MD +0.45 g/dL, 95% CI 0.05 to 0.85, p=0.03). The effect of non-pharmacological measures on the prevalence of IDA was analyzed in only 5 RCTs. Participants in the intervention groups were 2.78 times less likely to suffer from IDA than those in the control groups, OR=2.78, 95% CI 0.93, 8.29, however without significance for the overall effect (p=0.07).

Conclusion: Non-pharmacological therapies have a positive effect on iron balance, and can a useful adjunct to programs to prevent and treat IDA in at-risk populations. (PROSPERO registration number CRD42021261773).

Abbreviations used in manuscript

GRADE	Grading of Recommendations Assessment, Development and Evaluation
Hb	Hemoglobin
ID	Iron deficiency
IDA	Iron-deficiency anemia
MD	Mean difference
OR	Odds ratio
RCT	Randomized clinical trial
WHO	World Health Organization

Introduction

Anemia is an important indicator of malnutrition and health with great consequences for socioeconomic development. Children under two years of age with severe anemia are at higher risk of mortality, and even mild forms, which can be corrected, cause permanent cognitive damage by decreasing attention span and memory deficits.[1,2].

According to WHO estimates, between 1993 and 2005, anemia affected approximately a quarter of the world's population, which then corresponded to 1.62 billion people, the majority being children under the age of four years. A recent study showed a decrease in the prevalence of anemia between 1990 and 2010 from 40.2% to 32.9% of the world population, especially among men. The regions most affected by anemia were Southeast Asia and sub-Saharan Africa. Iron deficiency (ID) was the main cause, and children under the age of 5 years were most affected. Malaria, schistosomiasis and chronic renal failure were the causes of anemia for which prevalence most increased in this period.[3]

The Pan American Health Organization states that Brazil is in second place among countries in Latin America and the Caribbean with the highest prevalence of anemia (30%); only Peru has higher numbers with 57%.[4,5] According to the Brazilian Ministry of Health, in 2006, the general estimate of the prevalence of anemia in the country was 25 to 30%. In Brazil there is no official record of the prevalence of the disease; only regional studies can be found.[6-9]

Among the causes of anemia, ID is the most common, accounting for 50% of cases. In developing countries such as Brazil, diet has an important role in anemia caused by ID, mainly because iron, although present in cereals and legumes (foods that are easily accessed), its presence is in a low availability form. Therefore, in risk groups, it is necessary to stimulate the consumption of animal-based foods like meat and chicken, which contain an optimal amount of iron in its active form, to prevent iron- deficiency anemia (IDA).[5,8,10-13]

Currently, ID in Brazil is more common than other deficiencies, such as hypovitaminosis A, primary iodine deficiency, or protein-energy malnutrition. However, ID may also be the result of blood loss. While menstrual loss is the major non-nutritional cause of ID in women of childbearing age, in men and postmenopausal women, bleeding

from the gastrointestinal tract is frequent cause.[11,14]

Even today, despite numerous health policies developed by the WHO and other agencies, anemia is a highly prevalent pathology in Brazil and worldwide. It is important not to undervalue or trivialize the disease, even when it is mild and oligosymptomatic, given that socioeconomic, intellectual and quality of life losses may result from this problem. This is without considering the increase in mortality in biologically more fragile populations.[15]

A nutrition education strategy that aims at the adequate quantitative and qualitative consumption of foods that are sources of different nutrients is an alternative that has low cost and does not produce undesirable effects. Through this, it is possible to increase the population's knowledge about ID and clarify about monotonous and iron-poor diets, which constitute one of the main causes of this deficiency. It is noteworthy, however, that changes in eating habits are not quickly achieved, making the strategy effective in the long term. Intervention studies through educational actions aimed at parents of children under the age of 24 months were effective in preventing ID. These results confirm that adherence to correct dietary practices is important to address this problem, which presents high prevalence in this age group.[16] However, for positive results, their actions must guarantee the consumption of foods rich in iron and dietary strategies that increase the bioavailability of iron in the diet, in addition to reducing the factors that hinder it.

It is still uncertain whether non-pharmacological measures, including iron-rich foods, are able to prevent and treat anemia in vulnerable populations. Therefore, this study intends to evaluate the effectiveness of non-pharmacological measures for the prevention and treatment of IDA.

Methods

Study design

This is a systematic review and meta-analysis to verify the efficacy and safety of non-pharmacological measures for the treatment and prevention of IDA.

Definition of the clinical question

The definition of the specific question was carried out under the acronym PICOS, as shown in Figure 1.

[Figure 1 about here]

Information sources

To conduct this study, the MEDLINE (via PubMed), Cochrane library, SciELO/LILACS and EMBASE databases were used. They were searched with no date or language restrictions. In addition, the reference list of included studies was also manually searched by the reviewers. This review was designed and conducted in accordance with the PRISMA[17] guidelines and registered at PROSPERO under the registration number CRD42021261773.

Search

To retrieve the articles (last search date was June 2021) we used the Boolean operators OR and AND. For the SciELO/LILACS database, the operators (Anemia) AND (Food) were used. In the Cochrane library the search algorithms were (Anemia), (Food Intake), (Randomized Controlled Trial) inserted without modification. However, to perform the search in the MEDLINE (via PubMed) and EMBASE databases, the terms MeSH and EMTREE were inserted, respectively.

Therefore, to perform the PubMed search, the appropriate MeSH terms were searched first. When inserting the studied condition (Anemia) the platform generated the following term: "Anemia". For the term (Food Intake), the following were generated: (Intake, Food) OR (Nutrient Intake) OR (Intake, Nutrient) OR (Nutrient Intakes) OR (Nutritional Intake) OR (Intake, Nutritional) OR (Nutritional Intakes) OR (Dietary Intake) OR (Dietary Intakes) OR (Intake, Dietary) OR (Micronutrient Intake) OR (Intake, Micronutrient) OR (Micronutrient Intakes) OR (Ingestion) OR (Feed Intake) OR (Feed Intakes) OR (Intake, Feed) OR (Macronutrient Intake) OR (Intake, Macronutrient) OR (Macronutrient Intakes) OR (Calorie Intake) OR (Calorie Intakes) OR (Intake, Calorie) OR "Eating"[MeSH].

A randomized controlled trial filter[18] was used with the previously described MeSH terms: (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial" [tw]) OR ((singl* [tw] OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw])) OR ("latin square" [tw]) OR placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp] OR follow-up studies [mh] OR prospective studies [mh] OR cross-over studies [mh] OR control*[tw] OR

prospectiv* [tw] OR volunteer* [tw]) NOT (animal [mh] NOT human [mh]).

To search the EMBASE platform, in addition to the terms listed above, the EMTREE terms were used: 'iron deficiency anemia'/exp AND 'iron deficiency'/exp AND ('food intake'/exp OR 'appetite regulation' OR 'feed intake' OR 'feeding methods' OR 'food consumption' OR 'food intake' OR 'food intake' OR 'food intake regulation' OR 'food uptake' OR 'meal'.

In addition to this search strategy, a manual search was carried out to analyze the references cited in the selected articles to identify additional documents for review.

Study selection

Randomized controlled clinical trials (RCTs) that used non-pharmacological measures to treat IDA including iron pots, iron ingots, or food use were included. There was no age group restriction. We excluded studies that did not include any quantifiable data.

Data collection process and quality assessment

Data were extracted from the included studies in standardized tables by one reviewer and verified by a second. Data were collected on study title, 1st author, year of publication, country, objectives, number of participants, population, type of intervention and comparison, primary and secondary outcomes, and main results. Synthesized data from all studies included in this review are shown in Table 1.

[Table 1 about here]

The Cochrane Risk-of-Bias (RoB 2.0) tool (available via the Risk of Bias tools website: www.riskofbias.info) was used to assess the quality and risk of bias in the RCTs included in this review. This tool is structured into five domains, through which bias may be introduced into the result: 1) bias arising from the randomization process - used to generate the participants' allocation sequence, which should be random; 2) bias due to deviations from intended interventions – this domain concerns the patient and the study team not knowing (being "blind") to which group the patient was allocated and whether there were deviations from the proposed intervention that could affect the outcome; 3) bias due to missing outcome data - loss to follow-up of study participants and, in case of loss, the reason for its occurrence; 4) bias in measurement of the outcome – outcome variable assessment, participant, researcher or data collector do not know which group the

participants have been assigned to; and 5) bias in selection of the reported result - the possibility that the researchers assessed outcomes through multiple assessments, but reported only the most convenient one(s).

To assess the quality of evidence, the Grading of Recommendations Assessment, Development and Evaluation (GRADE)[20] was used, thus ensuring a systematic and transparent process in this systematic review process. This system classifies evidence into high, moderate, low or very low quality, considering all the factors that determine how reliable the results are. Two outcomes were evaluated, hemoglobin (Hb) concentrations, and prevalence of anemia.

Synthesis of results

Data was summarized and aggregated in a quantitative synthesis of the studies through a meta-analysis. Review Manager (RevMan)[21] statistical software, provided by Cochrane, was used to analyze data. Using the random-effects model of meta-analysis we assessed the magnitude of the intervention effects according to study outcomes in two graphs: 1) Hb index of all selected studies, subdivided into food and iron pot / iron ingot subgroups, further stratified to present data on children only using the same subdivisions; 2) prevalence of IDA, subdivided and stratified in the same manner. Data were summarized in a forest-plot type graph.

Results

Selection and characterization of studies

A total of 479 studies were retrieved from the databases (226 SciELO/LILACS; 207 MEDLINE (via PubMed); 29 in Cochrane Library; and 17 in EMBASE). Of these 4 duplicate records were removed. All titles and abstracts were reviewed and then 23 articles were read in full and reviewed for eligibility checking. Three articles met inclusion criteria. We also conducted a manual search for citations from the included articles to identify additional relevant studies, a further 8 records were identified. After these reports were screened for eligibility, all studies met inclusion criteria. Thus, eleven RCTs were included in this review (Figure 2).

[Figure 2 about here]

Risk of bias within studies

The quality of the included studies was independently assessed by two researchers (FMBG and FPNA) using the RoB 2.0 tool.[34] After initial analysis, discrepancies between items were discussed, and consensus was reached. In assessing the risk of bias, all outcomes (primary and secondary) were evaluated. Of the eleven studies evaluated in this review, 4 had low risk of bias, 4 had unclear risk of bias, and 3 had high risk of bias.

[Figure 3 about here]

Assessment of the quality of evidence according to GRADE

Included randomized studies had a low risk of bias and two outcomes were directly assessed: 1) differences in Hb levels (11 studies), 2) prevalence of anemia (five studies). Information bias was also unlikely. Regarding the analysis of the two outcomes, there was inconsistency in the results due to the participants' non-adherence to the proposed interventions. In the iron pots groups, use was not daily (average use was three times a week), and in the red meat group, mean consumption was less than half of what the intervention intended (0.7 dishes/day out of 2 dishes/day). Therefore, we consider the overall certainty of evidence to be moderate (Table 2).

[Table 2 about here]

Synthesis of results

Effect of using food and iron pots / ingots on hemoglobin levels

Estimates showed that the use of non-pharmacological measures was associated with a statistically significant overall increase in mean Hb (mean difference (MD) +0.45 g/dL, 95% CI 0.05 to 0.85, p=0.03), with a high level of heterogeneity among studies ($p<0.0001$, $I^2=91\%$). This mean increase in Hb concentrations was also present in the subgroups but without statistical significance (for the studies with food: MD +0.51 g/dL, 95% CI -0.32, 1.34, p=0.22) (for the studies with iron pots / ingots: MD +0.43 g/dL, 95% CI -0.06, 0.92, p=0.09) (Figure 4).

[Figure 4 about here]

Considering the studies conducted exclusively with children, the overall effect of non-pharmacological measures on Hb levels was statistically significant (p=0.01),

resulting in a mean increase of 0.69 g/dL (95% CI 0.15, 1.24), with a high level of heterogeneity (91%). In the subgroup analysis, only iron pots / ingots produced a significant rise (0.88 g/dL 95% CI 0.05, 1.72, p=0.04) in mean Hb values when compared to food (0.51 g/dL, 95% CI -0.32, 1.34, p=0.22) (Figure 5).

[Figure 5 about here]

Effect of use of food and iron pots / ingots on the prevalence of IDA

The effect of non-pharmacological measures on the prevalence of IDA was analyzed in only 5 RCTs. Participants in the intervention groups were 2.78 times less likely to suffer from IDA than those in the control groups, odds ratio (OR)=2.78, 95% CI 0.93, 8.29, with a high level of heterogeneity ($p<0.0001$, $I^2=90\%$), however without significance for the overall effect (p=0.07). In the subgroup analysis, participants in both the food and iron pots / ingots groups were less likely to be anemic when compared to control, OR=4.61, 95% CI 0.75, 28.50 and OR=1.99, 95% CI 0.47, 8.44, respectively, although once again without statistical significance (Figure 6).

[Figure 6 about here]

When analyzing changes in the prevalence of anemia only in children (3 trials), we found that participants in the interventions group were 3.20 times less likely to have IDA (OR=3.20, 95% CI 0.80, 12.80), without significance (p=0.10). In the food subgroup, IDA was less prevalent in the intervention group, as is the case with iron pots / ingots, although without statistical significance (p=0.10 and 0.50, respectively) (Figure 7).

[Figure 7 about here]

Discussion

Our systematic review showed that non-pharmacological treatments for IDA had a significant positive impact on Hb concentrations (MD +0.45 g/dL); however, in the subgroup (food or iron pots / ingots) analysis, although mean Hb values increased this was not statistically significant, probably due to a small subgroup size and a large confidence interval. This interval may result from the heterogeneity of the meta-

analysis, by combining studies with different methods, treatments used and target populations, but with a common objective. In the RCTs conducted exclusively with children, again the overall effect of non-pharmacological interventions provided a significant mean increase in Hb concentrations (0.69 g/dL). In the subgroup analyses, we found that iron pots / ingots impacted more significantly on mean Hb values than food (0.88 g/dL vs. 0.51 g/dL) in this population.

For the effect of food interventions on Hb concentrations, only 2 out of 3 interventions provided a positive effect.[28,33] In the study by Szymlek-Gay et al. (2009),[27] the authors reported that mean consumption (red meat intervention) was less than half of what the intervention intended (0.7 dishes/day out of 2 dishes/day), they recognized that identifying and removing factors that might have affected adherence could have delivered more effective results. Consequently, this study had a negative impact on the overall effect (MD -0.10, 95% CI -0.48, 0.28) of the studies.

The results of the interventions that used iron pots / ingots for cooking on Hb concentrations were extremely varied, in 5 out of 8 RCTS,[23,24,29,30,32] the effect of the intervention was superior to that of the control. Although, when analyzing the study by Talley et al. (2009), [29] we found that this study was carried out in different aid-dependent refugee camps where the prevalence of anemia had reduced significantly due to the distribution of a corn-soy blend prior to the intervention; furthermore, the authors believe that the response may also be due to lack of compliance with the Fe-alloy pots. The three remaining RCTs[25,26,31] reported negative effects on Hb values from the use of iron pots / ingots when compared with control. The study by Geerligs et al. (2003),[25] to assess the effect of cooking in iron pots with aluminum ones, was conducted in rural Malawian households. The authors attributed the inconsistent results of this study to high malaria parasite prevalence in the area. Nevertheless, they maintained the recommendation for this type of intervention. In the two other studies,[26,31] the results were inconclusive, and the authors recommended further studies on the bioavailability of this iron or the nonuse of these strategies.

However, in studies with children only, the use of iron pots / ingots provided a significant impact on Hb concentrations. For the three studies conducted in children only,[23,24,32] the authors considered this kind of intervention as a useful adjunct for programs to prevent IDA in at-risk populations, recommending their provision for households in less developed countries.

For the prevalence of anemia, we found that although participants in the intervention groups were less likely to suffer from IDA this probability was weakened due to the small number of trials with this outcome measure, and as consequence we were unable to confirm statistical significance (p=0.07 for all studies, and p=0.10 for studies performed with children). However, this outcome measure was only report in five studies.[26,28,30,32,33] The results of the food interventions[28,33] provided a greater impact on the prevalence of anemia, and participants in the intervention groups of these studies were 4.61 times less likely to suffer from IDA. The iron pots / ingots interventions[26,30,32] presented inclusive findings; in the study by Charles et al. (2015),[30] participants in the control group were about 4 times more likely to be anemic than those in the intervention groups; for Arcanjo et al. (2018),[32] there was little difference between the intervention and control groups, (reduction of prevalence of IDA from 10.7% to 8.4% in the intervention group, and 13.2% to 11.8% in the control group); but for Sharieff et al. (2007)[26] anemia was more prevalent in the intervention group when compared to the control group.

In studies with children only (three RCTs)[28,32,33] there was a reduction in the prevalence of IDA for studies with food interventions[28,33]; in one[28] the prevalence of anemia fell from 40% to 20% in the intervention group, with no change in the control group, while in the other[33] the prevalence of anemia fell from 36.8% to 15.8% in the intervention group, and rose from 16.7% to 25% in the control group. For the study with iron pots,[32] there was little difference between the intervention and control groups.

Strengths and limitations of the study

This systematic review evaluated the use of non-pharmacological measures on the prevention and treatment of anemia. These analyses examined the effect of sugar cane honey, brown sugar, red meat and cooking with iron pot or ingots on hemoglobin levels and the prevalence of anemia. To our knowledge, this is the first systematic review and meta-analysis aiming to understand the effect of alternative strategies for the treatment and prevention of IDA.

However, our review has limitations. First, few RCTs have investigated non-pharmacological measures, and the data available for the analysis of the study outcomes was limited. Second, some of the studies were conducted in populations with traditionally low Hb concentrations and high levels of anemia that were possible

involved in other nutrition programs at the time or shortly before the interventions. In addition, many of the studies presented large confidence intervals which prevented the authors from making a meaningful interpretation.

Conclusion

The evidence presented from the eleven RCTs included in this review suggest that these non-pharmacological therapies have a positive effect on iron balance, and can be defined as a useful adjunct to programs to prevent and treat ID in at-risk populations, especially those in low-income environments. The findings from this review show that there are therapeutic alternatives that do not include the use of drugs for the prevention and treatment of diseases related to nutritional deficiencies. The results of this review provide an evidence base for public health managers in the elaboration of public policies focused on this theme.

References

1. Soares Magalhães RJ, Clements AC. Spatial heterogeneity of haemoglobin concentration in preschool-age children in sub-Saharan Africa. Bull World Health Organ. 2011;89(6):459-468. doi:10.2471/BLT.10.083568
2. Central Statistical Agency [Ethiopia] and ICF International. Ethiopia Demographic and Health Survey 2011. Addis Ababa, Ethiopia and Calverton, Maryland, USA: Central Statistical Agency and ICF International; 2012.
3. Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood. 2014;123(5):615-624. doi:10.1182/blood-2013-06-508325
4. Amarante M, Otigossa A, Sueiro A, Oliveira C, Carvalho S. Anemia Ferropriva: uma visão atualizada. 2015;17(1):34–45.
5. Mujica-Coopman MF, Brito A, López de Romaña D, Ríos-Castillo I, Coris H, Olivares M. Prevalence of Anemia in Latin America and the Caribbean. Food Nutr Bull. 2015;36(2 Suppl):S119-S128. doi:10.1177/0379572115585775
6. Silla LM, Zelmanowicz A, Mito I, Michalowski M, Hellwing T, Shilling MA, et al. High prevalence of anemia in children and adult women in an urban population in southern Brazil. PLoS One. 2013;8(7):e68805. doi:10.1371/journal.pone.0068805

7. Corona LP, Duarte YA, Lebrão ML. Prevalence of anemia and associated factors in older adults: evidence from the SABE Study. Rev Saude Publica. 2014;48(5):723-431. doi:10.1590/s0034-8910.2014048005039
8. Borges RB, Weffort VRS. Anemia no Brasil – revisão [Anemia in Brazil – review]. Rev Med Minas Gerais. 2011;21(3 Supl 1):78–82.
9. Souza KJ, Tabox V de F, Oliveira JMC de, Pierezan MR, Giuffrida R, Bressa RC, et al. Perfil epidemiológico da anemia ferropriva no serviço de hematologia de um hospital público, estado de São Paulo, Brasil. Colloq Vitae. 2013;5(1):18– 28. doi: 10.5747/cv.2013.v005.n1
10. Fabian C, Olinto MT, Dias-da-Costa JS, Bairros F, Nácul LC. Prevalência de anemia e fatores associados em mulheres adultas residentes em São Leopoldo, Rio Grande do Sul, Brasil [Anemia prevalence and associated factors among adult women in São Leopoldo, Rio Grande do Sul, Brazil]. Cad Saude Publica. 2007;23(5):1199-1205. doi:10.1590/s0102-311x2007000500021
11. Cançado RD, Chiattone CS. Anemia ferropênica no adulto: causas, diagnóstico e tratamento [Iron deficiency anaemia in the adult: causes, diagnosis and treatment]. Rev Bras Hematol Hemoter. 2010;32(3):240–6. doi: 10.1590/S1516-84842010005000075
12. Lopez A, Cacoub P, Macdougall IC, Peyrin-Biroulet L. Iron deficiency anaemia. Lancet. 2016;387(10021):907-916. doi:10.1016/S0140-6736(15)60865-0
13. Bezerra AGN, Leal VS, Lira PIC de, Oliveira JS, Costa EC, Menezes RCE de, et al. Anemia and associated factors in women at reproductive age in a Brazilian Northeastern municipality. Anemia e fatores associados em mulheres de idade reprodutiva de um município do Nordeste brasileiro. Rev Bras Epidemiol. 2018;21:e180001. doi:10.1590/1980-549720180001
14. World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity: Vitamin and Mineral Nutrition Information System. Geneva: WHO; 2011. Available from: http://www.who.int/vmnis/indicators/haemoglobin.pdf
15. Silva JBCB da, Vieira GM. Epidemiological profile of anemia in hematology outpatient clinic in private health sector. Rev Med (São Paulo). 2021;100(1):20- 7. doi: 10.11606/issn.1679-9836.v100i1p20-27
16. Khoshnevisan F, Kimiagar M, Kalantaree N, Valaee N, Shaheedee N. Effect of

nutrition education and diet modification in iron depleted preschool children in nurseries in Tehran: a pilot study. Int J Vitam Nutr Res. 2004;74(4):264-268. doi:10.1024/0300-9831.74.4.264

17. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097
18. Robinson KA, Dickersin K. Development of a highly sensitive search strategy for the retrieval of reports of controlled trials using PubMed. Int J Epidemiol. 2002;31(1):150-153. doi:10.1093/ije/31.1.150
19. Schünemann HJ, Higgins JPT, Vist GE, Glasziou P, Akl EA, Skoetz N, et al. Chapter 14: Completing 'Summary of findings' tables and grading the certainty of the evidence. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021). London: Cochrane; 2021. Available from www.training.cochrane.org/handbook
20. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-926. doi:10.1136/bmj.39489.470347.AD
21. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration; 2014.
22. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi:10.1136/bmj.n71
23. Borigato EV, Martinez FE. Iron nutritional status is improved in Brazilian preterm infants fed food cooked in iron pots. J Nutr. 1998;128(5):855-859. doi:10.1093/jn/128.5.855
24. Adish AA, Esrey SA, Gyorkos TW, Jean-Baptiste J, Rojhani A. Effect of consumption of food cooked in iron pots on iron status and growth of young children: a randomised trial. Lancet. 1999;353(9154):712-716. doi:10.1016/S0140-6736(98)04450-X
25. Geerligs PP, Brabin B, Mkumbwa A, Broadhead R, Cuevas LE. The effect on haemoglobin of the use of iron cooking pots in rural Malawian households in an

area with high malaria prevalence: a randomized trial. Trop Med Int Health. 2003;8(4):310-315. doi:10.1046/j.1365-3156.2003.01023.x

26. Sharieff W, Dofonsou J, Zlotkin S. Is cooking food in iron pots an appropriate solution for the control of anaemia in developing countries? A randomised clinical trial in Benin. Public Health Nutr. 2008;11(9):971-977. doi:10.1017/S1368980007001139
27. Szymlek-Gay EA, Ferguson EL, Heath AL, Gray AR, Gibson RS. Food-based strategies improve iron status in toddlers: a randomized controlled trial12. Am J Clin Nutr. 2009;90(6):1541-1551. doi:10.3945/ajcn.2009.27588
28. Arcanjo FP, Pinto VP, Arcanjo MR, Amici MR, Amâncio OM. Effect of a beverage fortified with evaporated sugarcane juice on hemoglobin levels in preschool children. Rev Panam Salud Publica. 2009;26(4):350-354. doi:10.1590/s1020-49892009001000010
29. Talley L, Woodruff BA, Seal A, Tripp K, Mselle LS, Abdalla F, et al. Evaluation of the effectiveness of stainless steel cooking pots in reducing iron- deficiency anaemia in food aid-dependent populations [published correction appears in Public Health Nutr. 2010 Jan;13(1):145]. Public Health Nutr. 2010;13(1):107-115. doi:10.1017/S1368980009005254
30. Charles CV, Dewey CE, Daniell WE, Summerlee AJ. Iron-deficiency anaemia in rural Cambodia: community trial of a novel iron supplementation technique. Eur J Public Health. 2011;21(1):43-48. doi:10.1093/eurpub/ckp237
31. Rappaport AI, Whitfield KC, Chapman GE, Yada RY, Kheang KM, Louise J, et al. Randomized controlled trial assessing the efficacy of a reusable fish-shaped iron ingot to increase hemoglobin concentration in anemic, rural Cambodian women. Am J Clin Nutr. 2017;106(2):667-674. doi:10.3945/ajcn.117.152785
32. Arcanjo FPN, Macêdo DRR, Santos PR, Arcanjo CPC. Iron Pots for the Prevention and Treatment of Anemia in Preschoolers. Indian J Pediatr. 2018;85(8):625-631. doi:10.1007/s12098-017-2604-x
33. Arcanjo CC, Arcanjo FPN, Teixeira AA, Ponte YMG, Brito GA, Ferreira TP, Nascimento WMC, Santos PR. Sugar Cane Honey is as Effective as Weekly Iron Supplementation to Prevent and Treat Anemia in Preschoolers. International Journal of Health Sciences. 2020 Dez; 8(4):45-53. doi:10.15640/ijhs.v8n4a6
34. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB

2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. doi:10.1136/bmj.l4898

Table 1. Characterization of included randomized clinical trials.

1st Author/ Year of publication	Country	Number of participants	Population	Intervention	Comparison	Primary and secondary outcomes	Main results
Borigato (1998)[23]*	Brazil	45	Children between 4 and 12 months of age	Iron pots	Aluminum pots	Hemoglobin	Increase of 0.5g/dL in the intervention group and decrease of 0.7g/dL in the control group
Adish (1999)[24]*	Ethiopia	407	Children between 2 and 5 years of age	Iron pots	Aluminum / clay pots	Hemoglobin	Increase of 1.7g/dL in Hb levels in the intervention group; there was a difference in 1.3g/dL in Hb levels between the intervention and control groups
Geerligs (2003)[25]	Malawi	322	Adults and children over 1 year of age	Iron pots	Aluminum pots	Hemoglobin	0.68g/dL increase in Hb concentrations in children < 12 years and 0.53g/dL in those > 12 years, both considering groups with consistent use of the intervention; high proportion of malaria in blood samples, especially in children < 12 years
Sharieff (2007)[26]	Benin	339	Children (6-24 months), adolescents (11-15 years) and women (15-44 years)	Iron pots	Steel pots; iron supplementation	Hemoglobin; anemia	0.3g/dL increase in Hb values in the intervention group and 0.5g/dL in the control group; the effect on hematological indices was lower in the iron pot groups compared to the control groups that included the use of steel pots and iron supplementation
Szymlek-Gay (2009)[27]*	New Zealand	225	Children between 12 and 20 months of age	Red meat intake	Fortified milk; non-fortified milk	Hemoglobin; anemia	0.13g/dL increase in Hb levels in the intervention group and 0.23 in the group control; neither the red meat intervention nor the iron-fortified milk intervention was associated with a statistically significant change in anemia prevalence
Arcanjo (2009)[28]*	Brazil	352	Children between 2 and 3 years of age	Evaporated sugar cane juice	Refined sugar	Hemoglobin. anemia	Mean increase of 0.5 g/dL in Hb levels in the intervention group; reduction in the prevalence of anemia from 40% to 20% in the intervention group, remaining at 72.7%

1st Author/ Year of publication	Country	Number of participants	Population	Intervention	Comparison	Primary and secondary outcomes	Main results
Talley (2009)[29]	Tanzania	220	Children between 6 and 59 months of age and their mothers	Iron alloy pots	Aluminum / clay pots	Hemoglobin	in the control group Decrease in mean Hb concentrations of 0.2 g/dL in children 6 to 59 months of age and 0.6 g/dL in non-pregnant mothers in the intervention group; participants in the intervention group had lower iron levels than those in the control
Charles (2015)[30]	Cambodia	248	Women	Iron ingot	No intervention	Hemoglobin; anemia	Mean Hb increase of 1.3 g/dL in the intervention group and 0.1 g/dL in the control; participants in the control group were about 4 times more likely to be anemic than those in the intervention groups
Rappaport (2017)[31]	Cambodia	326	Women between 18 and 49 years of age	Iron ingot	No intervention	Hemoglobin	Decrease in mean Hb of 0.3 g/dL in the intervention group and 0.2 g/dL in the control group; there was no effect of the intervention on the prevalence of anemia
Arcanjo (2018)[32]*	Brazil	151	Children between 4 and 5 years of age	Iron pots	Aluminum pots	Hemoglobin; Anemia	Increase in Hb concentrations of 0.03 g/dL in the intervention group and a decrease of 0.2 g/dL in the control group; a reduction in the prevalence of anemia from 10.7% to 8.4% in the intervention group and from 13.2% to 11.8% in the control group
Arcanjo (2020)[33]*	Brazil	176	Children between 24 and 36 months of age	Sugar cane honey	Iron supplementation; no intervention	Hemoglobin; anemia	Increase of 0.5 g/dL in Hb levels in the intervention group and 0.74 g/dL decrease in the control group; prevalence of anemia fell from 36.8% to 15.8% in the intervention group, and rose from 16.7% to 25% in the control group

*Studies conducted only with children.

Table 2. A summary of findings table for evaluating the quality of evidence-non-pharmacological measures compared to control for hemoglobin concentrations and prevalence of anemia according to GRADE.

Certainty assessment							Summary of findings				
Nº of participants (studies) Follow up	Risk of bias	Inconsistency	Indirect evidence	Imprecision	Publication bias	Certainty of the evidence (GRADE)	Rate of events across studies (%)		Relative effect (95% CI)	Absolute estimates of effect	
							With control	With non-pharmacological measures		Risk with control	Risk differences with non-pharmacological measures
Hemoglobin concentrations											
2022 (11 RCTs)	not serious	serious [a]	not serious	not serious	none	⊕⊕⊕ MODERATE	980	1042	-	-	Mean **0.45 g/dL higher** (0.05 higher to 0.84 higher)
Prevalence of anemia							*No-prevalence of anemia*			*Prevalence of anemia*	
847 (5 RCTs)	not serious	serious [a]	not serious	not serious	none	⊕⊕⊕ MODERATE	208/369 (56.4%)	374/478 (78.2%)	**OR 2.78** (0.93, 8.29)	**436 per 1,000**	**219 fewer per 1,000** (156 fewer to 281 fewer)

CI: Confidence interval; **OR:** Odds ratio

[a] In some studies, the interventions did not follow what had been proposed, due to difficulty in adherence by the populations studied, despite this, the mean consumption and use of the approached methods were considered adequate for the researchers who studied them.

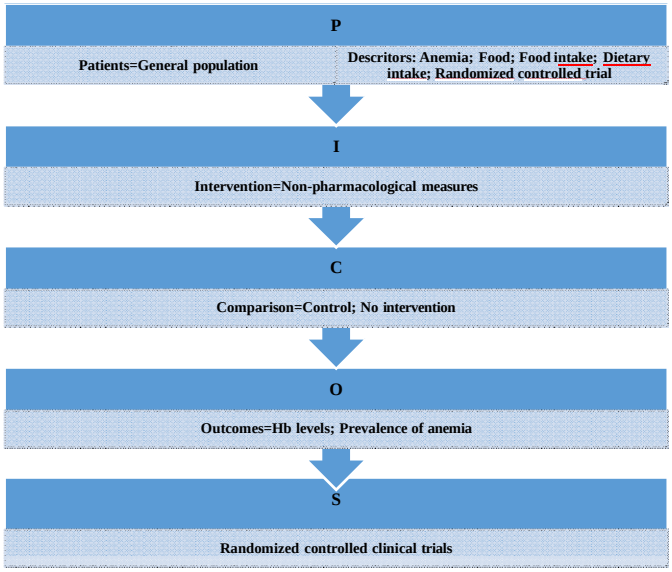


Figure 1. PICOS Question.

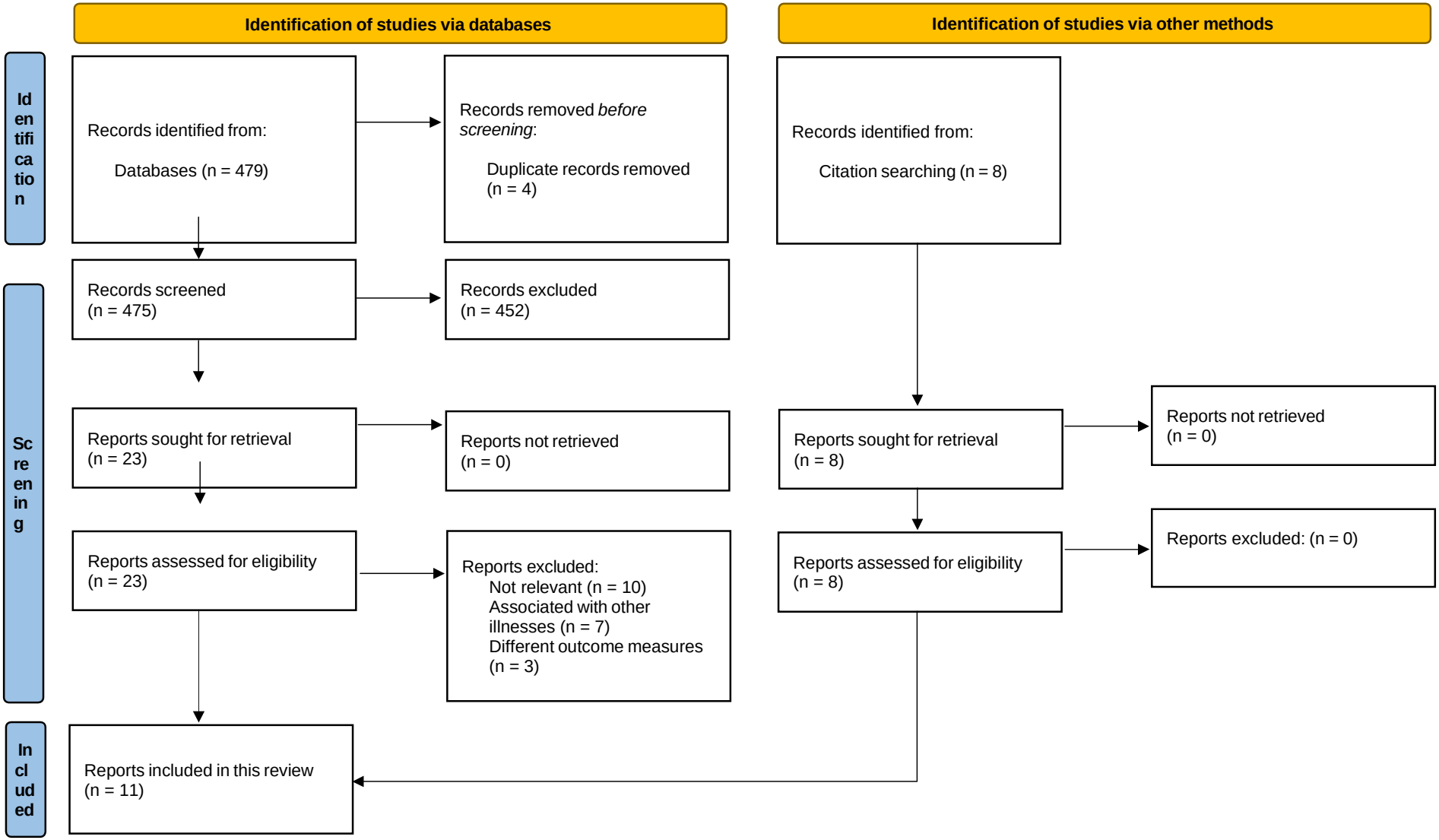


Figure 2. Search strategy according to the PRISMA protocol.[22]

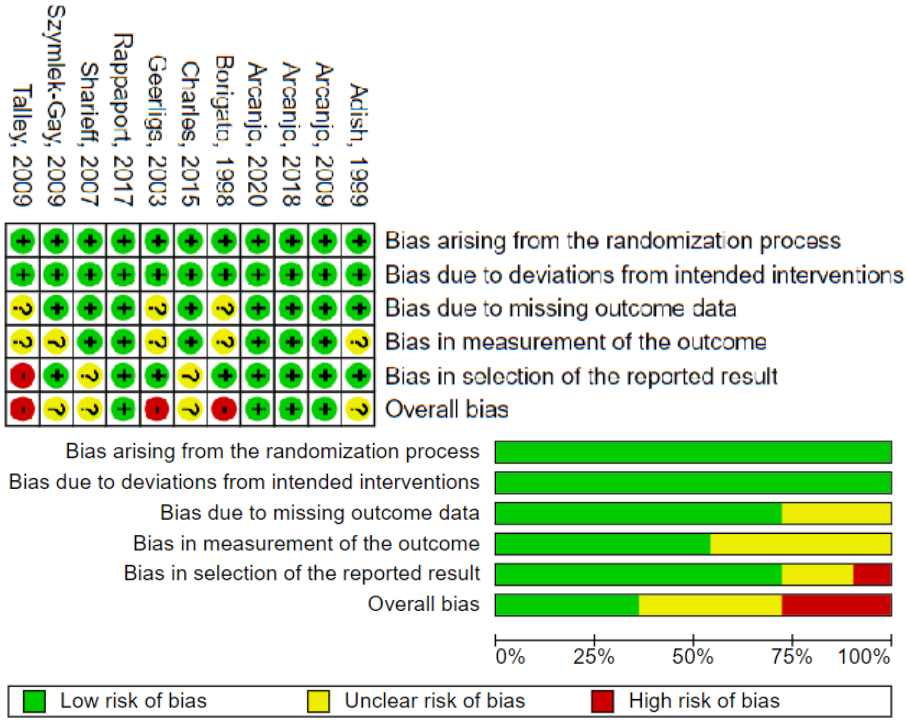


Figure 3. Risk of bias in studies using the Cochrane Risk of Bias tool (RoB 2.0).

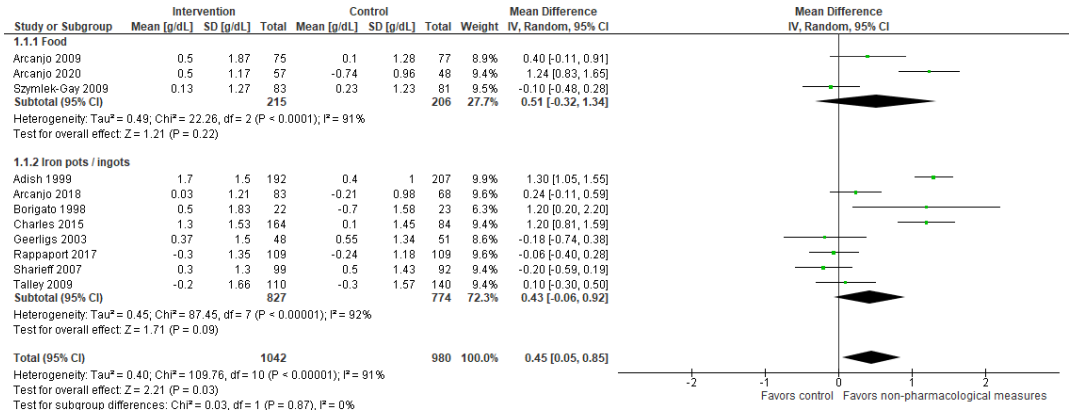


Figure 4. Effect for the overall and subgroup analysis of therapy with non-pharmacological measures on Hb levels.

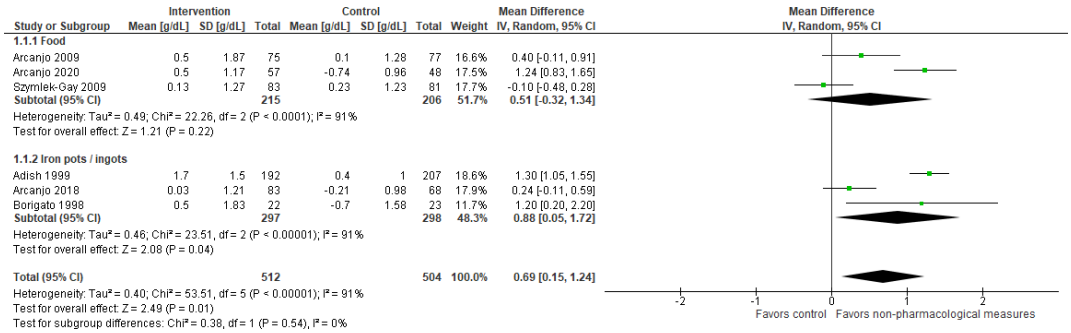


Figure 5. Effect for the overall and subgroup analysis of therapy with non-pharmacological measures on Hb levels in children.

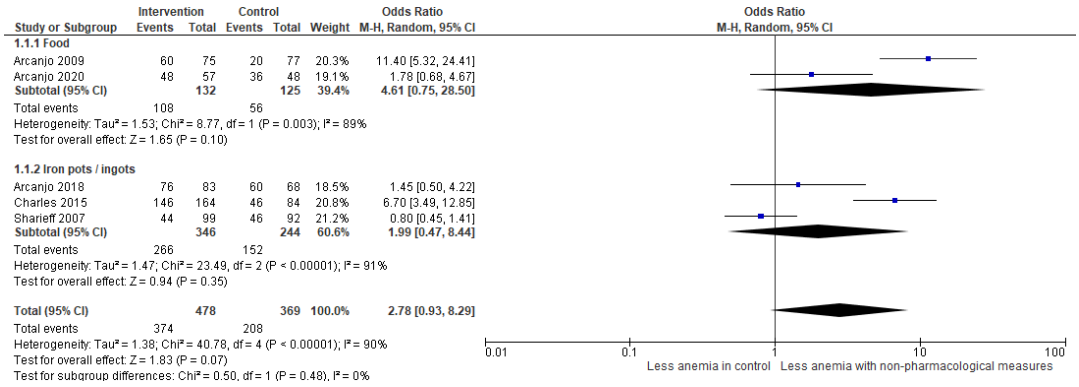


Figure 6. Effect for the overall and subgroup analysis of therapy with non-pharmacological measures on the prevalence of anemia.

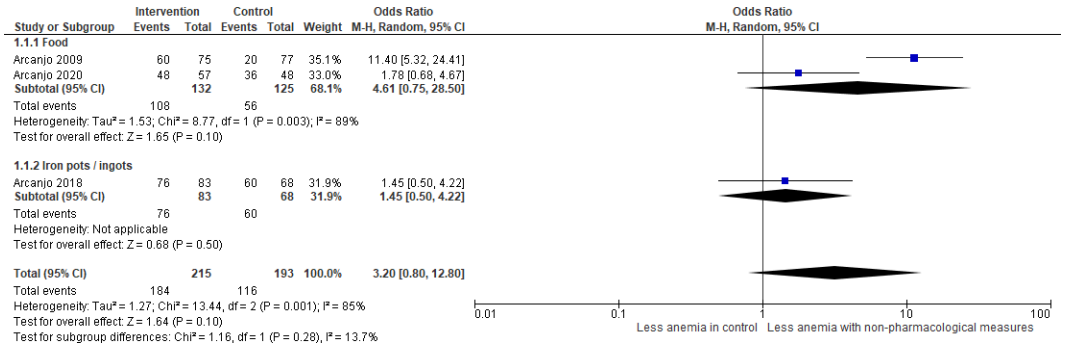


Figure 7. Effect for the overall and subgroup analysis of therapy with non-pharmacological measures on the prevalence of anemia in children.

REFERÊNCIAS

A ADISH, Abdulaziz et al. Effect of consumption of food cooked in iron pots on iron status and growth of young children: a randomised trial. **The Lancet**, [S.L.], v. 353, n. 9154, p. 712-716, fev. 1999. Elsevier BV. http://dx.doi.org/10.1016/s0140-6736(98)04450-x.

AMARANTE, Marla Karine *et al*. Anemia Ferropriva: uma visão atualizada. **Biosaúde**, Londrina, v. 17, n. 1, p. 34-45, 2015.

ARCANJO, Cecília Costa *et al*. Sugar Cane Honey is as Effective as Weekly Iron Supplementation to Prevent and Treat Anemia in Preschoolers. **International Journal Of Health Sciences**, [S.L.], v. 4, n. 8, p. 45-53, dez. 2020.

ARCANJO, Francisco P. *et al*. Effect of a beverage fortified with evaporated sugarcane juice on hemoglobin levels in preschool children. **Revista Panamericana de Salud Pública**, [S.L.], v. 26, n. 4, p. 350-354, out. 2009. FapUNIFESP (SciELO). http://dx.doi.org/10.1590/s1020-49892009001000010.

ARCANJO, Francisco Plácido Nogueira *et al*. Iron Pots for the Prevention and Treatment of Anemia in Preschoolers. **The Indian Journal Of Pediatrics**, [S.L.], v. 85, n. 8, p. 625-631, 11 jan. 2018. Springer Science and Business Media LLC. http://dx.doi.org/10.1007/s12098-017-2604-x.

A ROBINSON, Karen; DICKERSIN, Kay. Development of a highly sensitive search strategy for the retrieval of reports of controlled trials using PubMed. **International Journal Of Epidemiology**, [S.L.], v. 31, n. 1, p. 150-153, fev. 2002. Oxford University Press (OUP). http://dx.doi.org/10.1093/ije/31.1.150.

A SZYMLEK-GAY, Ewa *et al*. Food-based strategies improve iron status in toddlers: a randomized controlled trial. **The American Journal Of Clinical Nutrition**, [S.L.], v. 90, n. 6, p. 1541-1551, 14 out. 2009. Oxford University Press (OUP). http://dx.doi.org/10.3945/ajcn.2009.27588.

BARBOSA, Diana L.; ARRUDA, Ilma K. G.; DINIZ, Alcides S.. Prevalência e caracterização da anemia em idosos do Programa de Saúde da Família. **Revista Brasileira de Hematologia e Hemoterapia**, [S.L.], v. 28, n. 4, dez. 2006. Elsevier BV. http://dx.doi.org/10.1590/s1516-84842006000400014.

BEUTLER, Ernest et al. The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration?. **Blood**, [S.L.], v. 107, n. 5, p. 1747-1750, 1 mar. 2006. American Society of Hematology. http://dx.doi.org/10.1182/blood-2005-07-3046.

BEZERRA, Adriana Guimarães Negromonte *et al*. Anemia e fatores associados em mulheres de idade reprodutiva de um município do Nordeste brasileiro. **Revista Brasileira de Epidemiologia**, [S.L.], v. 21, 28 maio 2018. FapUNIFESP (SciELO). http://dx.doi.org/10.1590/1980-549720180001.

BORGES, Rosanea B; WELFORT, Virgínia R. Anemia no Brasil – revisão. **Rev Med Minas Gerais**. V. 21 (3 supl), p. 78-82, 2011; Disponível em: http://www.rmmg.org/sumario/75.

BORIGATO, Eliana V. M.; MARTINEZ, Francisco E.. Iron Nutritional Status Is Improved in Brazilian Preterm Infants Fed Food Cooked in Iron Pots. **The Journal Of Nutrition**, [S.L.], v. 128, n. 5, p. 855-859, 1 maio 1998. Oxford University Press (OUP). http://dx.doi.org/10.1093/jn/128.5.855.

BRASIL. Lei n° 11.346, de 15 de setembro de 2006. Lei Orgânica de Segurança Alimentar e Nutricional. Dispõe sobre a Criação do Sistema Nacional de Segurança Alimentar e Nutricional– SISAN com vistas em assegurar o direito humano à alimentação adequada e dá outras providências. **Diário Oficial da União** 2006; 18 set.

BRASIL. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Saúde da criança: aleitamento materno e alimentação complementar / Ministério da Saúde, Secretaria de Atenção à Saúde**, Departamento de Atenção Básica.** – 2. ed. Disponível em http://bvsms.saude.gov.br/ bvs/publicacoes/saude_crianca_aleitamento_ materno_cab23.pdf

CANÇADO, Rodolfo D.; CHIATTONE, Carlos S.. Anemia ferropênica no adulto: causas, diagnóstico e tratamento. **Revista Brasileira de Hematologia e Hemoterapia**, [S.L.], v. 32, n. 3, p. 240-246, 2010. Elsevier BV. http://dx.doi.org/10.1590/s1516-84842010005000075.

CENTRAL STATISTICAL AGENCY [ETHIOPIA], ICF INTERNATIONAL. Ethiopia Demographic and Health Survey 2011. Addis Ababa, Ethiopia and Calverton, Maryland, USA. **Central Statistical Agency and ICF International**; 2012.

CHAPARRO, Camila M.; SUCHDEV, Parminder S.. Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. **Annals Of The New York Academy Of Sciences**, [S.L.], 22 abr. 2019. Wiley. http://dx.doi.org/10.1111/nyas.14092.

CHARLES, Christopher V *et al*. A Randomized Control Trial Using a Fish-Shaped Iron Ingot for the Amelioration of Iron Deficiency Anemia in Rural Cambodian Women. **Tropical Medicine & Surgery**, [S.L.], v. 03, n. 03, 2015. OMICS Publishing Group. http://dx.doi.org/10.4172/2329-9088.1000195.

CORONA, Ligiana Pires; DUARTE, Yeda Aparecida de Oliveira; LEBRÃO, Maria Lucia. Prevalence of anemia and associated factors in older adults: evidence from the sabe study. **Revista de Saúde Pública**, [S.L.], v. 48, n. 5, p. 723-431, out. 2014. FapUNIFESP (SciELO). http://dx.doi.org/10.1590/s0034-8910.2014048005039.

DEPARTAMENTO DE AGRICULTURA DOS ESTADOS UNIDOS. Serviço de Pesquisa Agrícola: **National Nutrient Database for Standard Release de referência** 28, 2016 [Online]. Disponível: https: //data.nal.usda.gov/dataset/usda-national-nutrient-database-standard-reference-legacy-elease (5 de jun de 2020).

DEPARTAMENTO DE AGRICULTURA E AGRICULTURA DOS EUA. Serviço de pesquisa. Nutriente Nacional do USDA. **Banco de dados para referência padrão**, versão 14.

Washington: USDA-ARS; 2001.

FABIAN, Cristina *et al*. Prevalência de anemia e fatores associados em mulheres adultas residentes em São Leopoldo, Rio Grande do Sul, Brasil. **Cadernos de Saúde Pública**, [S.L.], v. 23, n. 5, p. 1199-1205, maio 2007. FapUNIFESP (SciELO). http://dx.doi.org/10.1590/s0102-311x2007000500021.

FISBERG, Mauro; LYRA, Isa; WEFFORT, Virginia. **CONSENSO SOBRE ANEMIA FERROPRIVA:** mais que uma doença, uma urgência médica!. 2. ed. São Paulo: Sociedade Brasileira de Pediatria - Departamentos de Nutrologia e Hematologia-Hemoterapia, 2018.

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS AND CAB INTERNATIONAL. Combating Micronutrient Deficiencies:Food-based Approaches. 2011. Edited by Brian Thompson and Leslie Amoroso. Available from www.fao.org/docrep/013/am027e/am027e00.htm (accessed 10 Jun 2021).

GEERLIGS, Paul Prinsen *et al*. The effect on haemoglobin of the use of iron cooking pots in rural Malawian households in an area with high malaria prevalence: a randomized trial. **Tropical Medicine And International Health**, [S.L.], v. 8, n. 4, p. 310-315, abr. 2003. Wiley. http://dx.doi.org/10.1046/j.1365-3156.2003.01023.x.

GRADE WORKING GROUP. **What is GRADE?** @2020. Disponível em: https://www.gradeworkinggroup.org/. Acesso em 15 mai. 2021.

GUYATT, Gordon H *et al*. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. **Bmj**, [S.L.], v. 336, n. 7650, p. 924-926, 24 abr. 2008. BMJ. http://dx.doi.org/10.1136/bmj.39489.470347.ad.

HASSAN, Tamer Hasan *et al*. Impact of iron deficiency anemia on the function of the immune system in children. **Medicine**, [S.L.], v. 95, n. 47, nov. 2016. Ovid Technologies (Wolters Kluwer Health). http://dx.doi.org/10.1097/md.0000000000005395.

HIGGINS, Julian Pt *et al*. Assessing risk of bias in a randomized trial. In: HIGGINS, Julian; THOMAS, James. **Cochrane Handbook for Systematic Reviews of Interventions**. 6.2. Cochrane Training, 2021. Cap. 8. Disponível em: https://training.cochrane.org/handbook/current/chapter-08. Acesso em: 23 jun. 2021. https://www.gradeworkinggroup.org/. Acesso em 23 jun. 2021.

KASSEBAUM, Nicholas J. et al. A systematic analysis of global anemia burden from 1990 to 2010. **Blood**, [S.L.], v. 123, n. 5, p. 615-624, 30 jan. 2014. American Society of Hematology. http://dx.doi.org/10.1182/blood-2013-06-508325.

KHOSHNEVISAN *et al*. Effect of Nutrition Education and Diet Modification in Iron Depleted Preschool Children in Nurseries in Tehran: a pilot study. **International Journal For Vitamin And Nutrition Research**, [S.L.], v. 74, n. 4, p. 264-268, 1 jul. 2004. Hogrefe Publishing Group. http://dx.doi.org/10.1024/0300-9831.74.4.264.

LIBERATI, Alessandro *et al*. The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: explanation and elaboration. **Plos Medicine**, [S.L.], v. 6, n. 7, p. 0-1, jul. 2009. Public Library of Science (PLoS). http://dx.doi.org/10.1371/journal.pmed.1000100.t001.

LOPES, Davi Lima *et al*. ASPECTOS CLINICOS PERTINENTES NA ANEMIA FERROPRIVA EM CRIANÇAS. **Mostra Científica em Biomedicina**, Quixadá, v. 3, n. 2, 2019.

LOPEZ, Anthony *et al*. Iron deficiency anaemia. **The Lancet**, [S.L.], v. 387, n. 10021, p. 907-916, fev. 2016. Elsevier BV. http://dx.doi.org/10.1016/s0140-6736(15)60865-0.

MA, Qiuyue *et al*. Study on the Prevalence of Severe Anemia among Non-Pregnant Women of Reproductive Age in Rural China: a large population-based cross-sectional study. **Nutrients**, [S.L.], v. 9, n. 12, p. 1298, 28 nov. 2017. MDPI AG. http://dx.doi.org/10.3390/nu9121298.

MAGALHÃES, Ricardo J Soares; CLEMENTS, Archie Ca. Spatial heterogeneity of haemoglobin concentration in preschool-age children in sub-Saharan Africa. **Bulletin Of The World Health Organization**, [S.L.], v. 89, n. 6, p. 459-468, 1 jun. 2011. WHO Press. http://dx.doi.org/10.2471/blt.10.083568.

MORAIS, Dayane de Castro *et al*. Insegurança alimentar e indicadores antropométricos, dietéticos e sociais em estudos brasileiros: uma revisão sistemática. **Ciência & Saúde Coletiva**, [S.L.], v. 19, n. 5, p. 1475-1488, maio 2014. FapUNIFESP (SciELO). http://dx.doi.org/10.1590/1413-81232014195.13012013.

MUJICA-COOPMAN, María F. *et al*. Prevalence of Anemia in Latin America and the Caribbean. **Food And Nutrition Bulletin**, [S.L.], v. 36, n. 2, p. 119-128, jun. 2015. SAGE Publications. http://dx.doi.org/10.1177/0379572115585775.

NAFIL, H.; TAZI, I.; MAHMAL, L.. Prevalence of pica in iron deficiency anemia in Marrakech (Morocco). **Médecine Et Santé Tropicales**, [S.L.], v. 25, n. 3, p. 273-275, jul. 2015. John Libbey Eurotext. http://dx.doi.org/10.1684/mst.2013.0199.

OLIVEIRA, Juliana Souza *et al*. Insegurança alimentar e estado nutricional de crianças de Gameleira, zona da mata do Nordeste brasileiro. **Revista Brasileira de Saúde Materno Infantil**, [S.L.], v. 10, n. 2, p. 237-245, jun. 2010. FapUNIFESP (SciELO). http://dx.doi.org/10.1590/s1519-38292010000200011.

OSUNGBADE, Kayode; OLADUNJOYE, Adeolu. Anaemia in Developing Countries: burden and prospects of prevention and control. **Anemia**, [S.L.], 29 fev. 2012. InTech. http://dx.doi.org/10.5772/29148.

RAPPAPORT, Aviva I *et al*. Randomized controlled trial assessing the efficacy of a reusable fish-shaped iron ingot to increase hemoglobin concentration in anemic, rural Cambodian women. **The American Journal Of Clinical Nutrition**, [S.L.], v. 106, n. 2, p. 667-674, 14 jun. 2017. Oxford University Press (OUP). http://dx.doi.org/10.3945/ajcn.117.152785.

REVIEW MANAGER (RevMan) [programa de computador]. Versão 5.3. Copenhagen, o Nordic Cochrane Center; 2014.

RISK OF BIAS 2.0. CRG STARTER PACK. Llll: **Cochrane Handbook**, 2020.

SANTIS, Gil Cunha de et al. Anemia. **Medicina (Ribeirao Preto Online)**, [S.L.], v. 52, n. 3, p. 239-251, 7 nov. 2019. Universidade de Sao Paulo, Agencia USP de Gestao da Informacao Academica (AGUIA). http://dx.doi.org/10.11606/issn.2176-7262.v52i3p239-251.

SCHÜNEMANN, Holger J *et al*. Completing 'Summary of findings' tables and grading the certainty of the evidence. In: HIGGINS, Julian. **Cochrane Handbook for Systematic Reviews of Interventions**. 6.2; Cochrane Training, 2021. Cap. 14. Disponível em: https://training.cochrane.org/handbook/current/chapter-14. Acesso em: 23 jun. 2021.

SHARIEFF, Waseem; DOFONSOU, Joyce; ZLOTKIN, Stanley. Is cooking food in iron pots an appropriate solution for the control of anaemia in developing countries? A randomised clinical trial in Benin. **Public Health Nutrition**, [S.L.], v. 11, n. 9, p. 971-977, set. 2008. Cambridge University Press (CUP). http://dx.doi.org/10.1017/s1368980007001139.

SILLA, Lucia Mariano da Rocha et al. High Prevalence of Anemia in Children and Adult Women in an Urban Population in Southern Brazil. **Plos One**, [S.L.], v. 8, n. 7, 29 jul. 2013. Public Library of Science (PLoS). http://dx.doi.org/10.1371/journal.pone.0068805.

SILVA, Jiviane B.; VIEIRA, Gabriel M. Perfil epidemiológico da anemia em ambulatório de hematologia da rede privada de saúde. **Revista De Medicina**, v. 1, n 1, p. 20-27, 2021. https://doi.org/10.11606/issn.1679-9836.v100i1p20-27

SILVA, Mariane Alves *et al*. Prevalência e fatores associados à anemia ferropriva e hipovitaminose A em crianças menores de um ano. **Cadernos Saúde Coletiva**, [S.L.], v. 23, n. 4, p. 362-367, dez. 2015. FapUNIFESP (SciELO). http://dx.doi.org/10.1590/1414-462x2015000100047.

SOCIEDADE BRASILEIRA DE PEDIATRIA. Manual de orientação para a alimentação do lactente, do pré-escolar, do escolar, do adolescente e na escola/Sociedade Brasileira de Pediatria**. Departamento de Nutrologia**. Disponível em http://www.sbp.com.br/fi leadmin/user_ upload/pdfs/14617a-PDManualNutrologiaAliment

SOUZA, Kleber Jordão *et al*. Perfil epidemiológico da anemia ferropriva no serviço de hematologia de um hospital público, estado de São Paulo, Brasil. **Colloquium Vitae**, [S.L.], v. 5, n. 1, p. 18-28, 30 jun. 2013. Associacao Prudentina de Educacao e Cultura (APEC). http://dx.doi.org/10.5747/cv.2013.v005.n1.v072.

TALLEY, Leisel *et al*. Evaluation of the effectiveness of stainless steel cooking pots in reducing iron-deficiency anaemia in food aid-dependent populations. **Public Health Nutrition**, [S.L.], v. 13, n. 1, p. 107-115, 1 abr. 2009. Cambridge University Press (CUP). http://dx.doi.org/10.1017/s1368980009005254.

TETTAMANTI, M. *et al*. Prevalence, incidence and types of mild anemia in the elderly: the. **Haematologica**, [S.L.], v. 95, n. 11, p. 1849-1856, 9 jun. 2010. Ferrata Storti Foundation (Haematologica). http://dx.doi.org/10.3324/haematol.2010.023101.

WORLD HEALTH ORGANISATION (WHO). Iron Deficiency Anaemia - Assessment, Prevention and Control. **A guide for programme managers**. World Health Organisation: WHO/NHD/01.3; 2001.

WORLD HEALTH ORGANIZATION (WHO), Food and Agricultural Organization of the United Nations. **Guidelines on Food Fortification with Micronutrients** *ISBN: 92 4 159401 2*. Allen L, de Benoist B, Dary O, Hurrell R edition. WHO, 2006. Available from www.who.int/nutrition/publications/micronutrients/9241594012/en/.

WORLD HEALTH ORGANIZATION (WHO). Vitamin and Mineral Nutrition Information System. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Geneve: **World Health Organization**; 2011. (WHO/NMH/NHD/MNM/11.1). http://www.who.int/vmnis/indicators/haemoglobin.pdf.

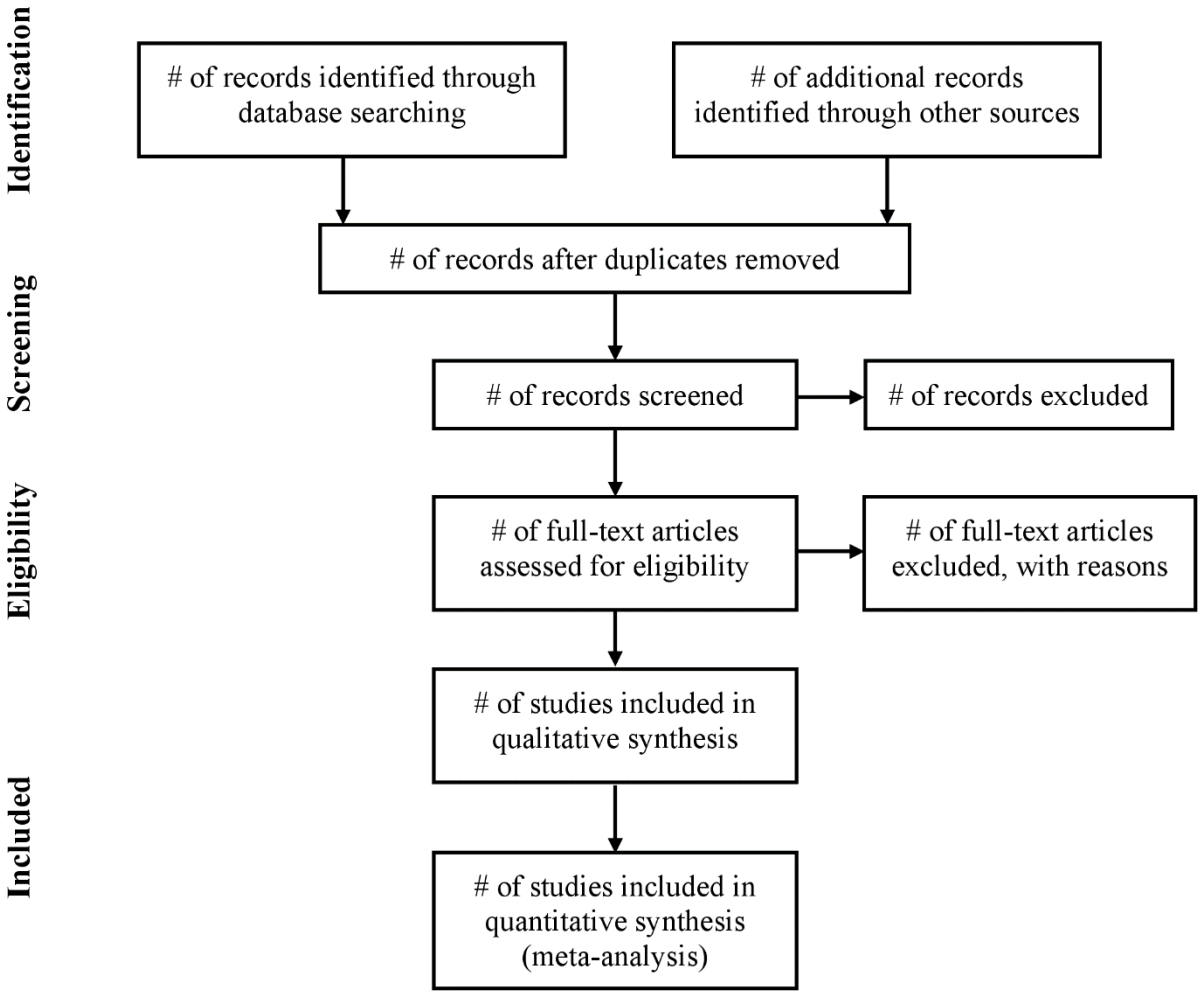
WORLD HEALTH ORGANIZATION (WHO). Documento final de la Segunda Conferencia Internacional sobre Nutrición: Declaracion de Roma sobre la Nutrición. Roma: **WHO;** 2014.

WORLD HEALTH ORGANIZATION (WHO). Nutritional Anaemias: **Tools for Effective Prevention and Control.** Available at: apps.who.int/nutrition/publications/micronutrients/anaemias-tools-prevention-control/en/index.html2017.

WORLD HEALTH ORGANIZATION. The prevalence of anaemia through primary health care: a guide for health administrators and programme managers. Geneva: Demayer EM e cols. **World Health Organization**, 1989.

ANEXOS

Anexo A - Fluxo de informações nas diferentes fases de uma revisão sistemática.



Fonte: The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration

MATERIAL SUPLEMENTAR

Material suplementar A – Protocolo de registro de Revisão Sistemática no International prospective register of systematic reviews (PROSPERO).

PROSPERO
International prospective register of systematic reviews

NHS
National Institute for Health Research

UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

[1*Review] title.

Give the title of the review in English

Treatment of ferroprivate anemia with non-pharmacological measures: systematic review and meta-analysis

2. Original language title.

For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

Pode-se tratar anemia com medidas não-farmacológicas?

3. * Anticipated or actual start date.

Give the date the systematic review started or is expected to start.

17/06/2021

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

17/10/2021

5. * Stage of review at time of this submission.

This field uses answers to initial screening questions. It cannot be edited until after registration.

Tick the boxes to show which review tasks have been started and which have been completed.

Update this field each time any amendments are made to a published record.

The review has not yet started: No

PROSPERO
International prospective register of systematic reviews

NHS National Institute for Health Research

Review stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	No	No
Risk of bias (quality) assessment	Yes	No
Data analysis	Yes	No

Provide any other relevant information about the stage of the review here.

6. * Named contact.

The named contact is the guarantor for the accuracy of the information in the register record. This may be any member of the review team.

Mayara Brasileiro

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Mrs Brasileiro

7. * Named contact email.

Give the electronic email address of the named contact.

mayarabrasileiro09@gmail.com

8. Named contact address

Give the full institutional/organisational postal address for the named contact.

Rua Vicente Linhares, 1550. Aldeota, CearÃ¡ - Brasil.

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

55(88) 9 9944-4963

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Universidade Federal do CearÃ¡

Organisation web address:

11. * Review team members and their organisational affiliations.

PROSPERO
International prospective register of systematic reviews

NHS
National Institute for Health Research

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country now MUST be entered for each person, unless you are amending a published record.**

Mrs Mayara Brasileiro. Universidade Federal do Ceara
Dr Francisco Arcanjo. Universidade Federal do Ceara

12. * Funding sources/sponsors.

Details of the individuals, organizations, groups, companies or other legal entities who have funded or sponsored the review.

Programa de Pós-graduação strictu sensu em Saúde da Família da Universidade Federal do Ceará - Campus Sobral

Grant number(s)

State the funder, grant or award number and the date of award

13. * Conflicts of interest.

List actual or perceived conflicts of interest (financial or academic).

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country must be completed for each person, unless you are amending a published record.**

15. * Review question.

State the review question(s) clearly and precisely. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS or similar where relevant.

Is there scientific evidence related to the treatment of anemia through non-pharmacological measures?

16. * Searches.

State the sources that will be searched (e.g. Medline). Give the search dates, and any restrictions (e.g. language or publication date). Do NOT enter the full search strategy (it may be provided as a link or attachment below.)

PubMed, Embase, Cochrane

17. URL to search strategy.

Upload a file with your search strategy, or an example of a search strategy for a specific database, (including the keywords) in pdf or word format. In doing so you are consenting to the file being made publicly accessible. Or provide a URL or link to the strategy. Do NOT provide links to your search **results**.

https://www.crd.york.ac.uk/PROSPEROFILES/261773_STRATEGY_20210618.pdf

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

PROSPERO
International prospective register of systematic reviews

NHS
National Institute for Health Research

Give a short description of the disease, condition or healthcare domain being studied in your systematic review.

Anemia is defined as a pathological process in which the concentration of hemoglobin "Hb", contained in red blood cells, is normally low, respecting the variations according to age, sex and altitude in relation to sea level, as a result of various situations such as chronic infections, hereditary blood problems, lack of one or more essential nutrients needed in storage such as ferritin and hemosiderin in the liver, spleen and bone marrow.

Iron deficiency and iron deficiency anemia, due to their high prevalence, repercussions on growth and development, resistance to infections and association with mortality in children under 2 years of age, are considered one of the main public health problems. most common nutritional in the world.

19. * Participants/population.

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

The general population, excluding those with severe anemia and other serious illnesses

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the interventions or the exposures to be reviewed. The preferred format includes details of both inclusion and exclusion criteria.

For selection of articles, the following inclusion criteria were used: studies with randomized clinical trials with a control group, whose intervention used iron pans or ingots and food, to reduce iron deficiency anemia, and that answered the following PICOT question : Is there scientific evidence related to the treatment of anemia through non-pharmacological measures? The Rayyan® reference manager was used as an aid. The exclusion criteria used were: duplicate articles, intervention or observational articles, and that did not respond to the research object. Groups that had the intervention were evaluated as a type of comparison with those that had none or another type of intervention.

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the intervention/exposure will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

2. In studies with iron cookware: comparison groups with stainless steel cookware;

3. In a study using red meat: comparison with fortified and unfortified milk.

22. * Types of study to be included.

Give details of the study designs (e.g. RCT) that are eligible for inclusion in the review. The preferred format includes both inclusion and exclusion criteria. If there are no restrictions on the types of study, this should be stated.

Randomized clinical trials with a control group, whose intervention used iron pans or ingots and food, to reduce iron deficiency anemia.

23. Context.

Give summary details of the setting or other relevant characteristics, which help define the inclusion or exclusion criteria.

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

The studies were analyzed from the extracted information, exposed through the instrument in the form of charts and tables, in order to provide greater clarity of the results, being organized with synthesized data from each article found, such as: name of the article, main author , year, objectives, type of study, number of participants, age of participants, intervention, duration of intervention and analyzed outcomes. They will be analyzed through meta-analysis using the Revman program and also risk of bias analysis using Cochrane's Risk of Bias (ROB 2.0). For methodological quality, we will use GRADE.

Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

In the studies that used iron pans and iron ingots, some had increased hemoglobin levels, in others the Fifteen studies that used iron, ne, brown sugar and red meat in comparison with the control group, there were significant differences in hemoglobin indices and in the prevalence of anemia, and research on the subject was considered relevant.

Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

The studies will be analyzed from the extracted information, displayed through the instrument in the form of tables and tables, in order to provide greater clarity of the results, being organized with synthesized data from each article found, such as: name of the article, main author , year, objectives, type of study, number of participants, age of participants, intervention, duration of the intervention and analyzed outcomes. The hemoglobin indices and prevalence of anemia in the populations studied will be used as data for the formation of tables and meta-analyses.

27. * Risk of bias (quality) assessment.

State which characteristics of the studies will be assessed and/or any formal risk of bias/quality assessment tools that will be used.

The risk of bias provided by Cochrane (ROB 2.0) and GRADE will be used to assess the quality of the studies and their methodologies.

28. * Strategy for data synthesis.

Describe the methods you plan to use to synthesise data. This **must not be generic text** but should be **specific to your review** and describe how the proposed approach will be applied to your data. If meta-analysis is planned, describe the models to be used, methods to explore statistical heterogeneity, and software package to be used.

A) Hemoglobin values in 11 selected articles;

2) Prevalence of anemia in 06 articles, among 11, that analyzed this variable for Non-pharmacological measures vs. Control for treating anemia.

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

The study will analyze groups of people, the general population, anemic and non-anemic, analyzing hemoglobin indices and anemia prevalence. Intervention groups and control groups (with different intervention or without intervention) will be evaluated; interventions consist of eating red meat, using sugar cane or sugar syrup, and using iron pans to cook food. Both with the aim of analyzing non-pharmacological measures for the treatment of anemia.

30. * Type and method of review.

Select the type of review, review method and health area from the lists below.

Type of review

Cost effectiveness
No

Diagnostic
No

Epidemiologic
No

Individual patient data (IPD) meta-analysis
No

Intervention
No

Living systematic review
No

Meta-analysis
Yes

Methodology
No

Narrative synthesis
No

Network meta-analysis
No

Pre-clinical
No

Prevention
No

Prognostic
No

Prospective meta-analysis (PMA)
No

Review of reviews
No

Service delivery
No

Synthesis of qualitative studies
No

Systematic review
Yes

Other
No

Health area of the review

Alcohol/substance misuse/abuse
No

Blood and immune system
Yes

Cancer
No

Cardiovascular
No

Care of the elderly
No

Child health
No

Complementary therapies
No

COVID-19
No

Crime and justice
No

Dental

No

Digestive system
No

Ear, nose and throat
No

Education
No

Endocrine and metabolic disorders
No

Eye disorders
No

General interest
No

Genetics
No

Health inequalities/health equity
No

Infections and infestations
No

International development
No

Mental health and behavioural conditions
No

Musculoskeletal
No

Neurological
No

Nursing
No

Obstetrics and gynaecology
No

Oral health
No

Palliative care
No

Perioperative care
No

Physiotherapy
No

Pregnancy and childbirth
No

Public health (including social determinants of health)
No

Rehabilitation
No

Respiratory disorders
No

Service delivery
No

Skin disorders
No

Social care
No

Surgery
No

Tropical Medicine
No

Urological
No

Wounds, injuries and accidents
No

Violence and abuse
No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.
English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out. For multi-national collaborations select all the countries involved.

Brazil

33. Other registration details.

Name any other organisation where the systematic review title or protocol is registered (e.g. Campbell, or The Joanna Briggs Institute) together with any unique identification number assigned by them. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

There is no registration in another institution

34. Reference and/or URL for published protocol.

If the protocol for this review is published provide details (authors, title and journal details, preferably in Vancouver format)

Add web link to the published protocol.

Or, upload your published protocol here in pdf format. Note that the upload will be publicly accessible.

PROSPERO
International prospective register of systematic reviews

NHS
National Institute for Health Research

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Do you intend to publish the review on completion?

Yes

Give brief details of plans for communicating review findings.?

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords help PROSPERO users find your review (keywords do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

"Anemia"; "Food Intake"; "Intake, Food"; "Nutrient Intake"; "Intake, Nutrient"; "Nutrient Intakes"; "Preschool Child"; "Children, Preschool"; "Preschool Children"; "randomized controlled trial"; "controlled clinical trial"; "randomized controlled trials"; "clinical trials"; "clinical trial";

37. Details of any existing review of the same topic by the same authors.

If you are registering an update of an existing review give details of the earlier versions and include a full bibliographic reference, if available.

38. * Current review status.

Update review status when the review is completed and when it is published.New registrations must be ongoing so this field is not editable for initial submission.
Please provide anticipated publication date

Review_Ongoing

39. Any additional information.

Provide any other information relevant to the registration of this review.

40. Details of final report/publication(s) or preprints if available.

Leave empty until publication details are available OR you have a link to a preprint (NOTE: this field is not editable for initial submission). List authors, title and journal details preferably in Vancouver format.

Give the link to the published review or preprint.