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SYSTEMATIC REVIEW AND META-ANALYSIS

Avoidant/restrictive food intake disorder: pediatric comorbidities

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Abstract

Introduction and Objectives: Avoidant/Restrictive Food Intake Disorder (ARFID) is a newly-recognized feeding and eating disorder diagnosis in the DSM-5 (2013) and ICD-11 (2019). This systematic review aims to gather knowledge on prevalent comorbidities in pediatric ARFID patients. **Methods:** Following PRISMA guidelines, a systematic literature review was conducted, focusing on comorbidities in ARFID-diagnosed participants with a mean age inferior or equal to 18 years old. Covering the period from 2013 to September 2023, a search across PubMed and B-On resulted in 20 selected studies from an initial pool of 161 articles. The risk of bias was assessed using the ROBINS-I tool. PROSPERO CRD42024503067. **Results:** Medical comorbidities were detailed in eight studies, revealing that 38% of the comorbidities observed were gastrointestinal symptoms, 25% neurological conditions, and 10% immune system complications. Psychiatric comorbidities were addressed in most of the studies, with 45% of observations displaying anxiety disorders, 33% neurodevelopmental disorders, and 15% mood disorders. Various other medical and psychiatric conditions were also identified. **Discussion:** This review underscores the association between ARFID and diverse comorbidities, including gastrointestinal, neurological, and psychiatric conditions. It highlights the disorder's complexity and the increased medical risks, advocating for early, multidisciplinary interventions and greater awareness among educators and health professionals. The need for comprehensive treatment involving various medical specialists is emphasized, along with the importance of family involvement and further research to enhance understanding and treatment of ARFID.

Keywords: Avoidant restrictive food intake disorder. Comorbidity. Child. Adolescent.

Transtorno evitativo/restritivo da ingestão de alimentos: comorbidades pediátricas

Resumo

Introdução e Objetivos: Perturbação de Ingestão Alimentar Evitativa/Restritiva (ARFID) é um diagnóstico de perturbação alimentar reconhecido recentemente no DSM-5 (2013) e CID-11 (2019). Esta revisão sistemática tem como objetivo reunir conhecimento sobre as comorbilidades mais prevalentes em doentes pediátricos com ARFID. **Métodos:** Seguindo as guidelines PRISMA, foi realizada uma revisão sistemática da literatura focada nas comorbilidades em participantes diagnosticados com ARFID com uma média de idades inferior ou igual a 18 anos. Abrangendo o período de 2013 a setembro de 2023, uma pesquisa na PubMed e B-On resultou em 20 estudos selecionados de um conjunto inicial de 161. O risco de viés foi analisado utilizando a ferramenta ROBINS-I. PROSPERO CRD42024503067. **Resultados:** As comorbilidades médicas foram detalhadas em 8 estudos, revelando que 38% das comorbilidades observadas eram sintomas gastrointestinais, 25% problemas neurológicos e 10% complicações do

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sistema imunitário. As comorbilidades psiquiátricas foram abordadas na maioria dos estudos, com 45% das observações a revelar perturbações de ansiedade, 33% perturbações do neurodesenvolvimento e 15% perturbações do humor. Também foram identificadas outras condições médicas e psiquiátricas. **Discussão:** Esta revisão sublinha a associação entre ARFID e diversas comorbilidades, incluindo doenças gastrointestinais, neurológicas e psiquiátricas. Destaca a complexidade da doença e o aumento dos riscos médicos, defendendo intervenções precoces e multidisciplinares e uma maior consciencialização dos educadores e profissionais de saúde. É realçada a necessidade de um tratamento abrangente que envolva vários médicos especialistas, bem como a importância do envolvimento da família e de mais investigação para melhorar a compreensão e o tratamento da doença.

Palavras-chave: Perturbação de ingestão alimentar evitante/restritiva. Comorbilidades. Crianças. Adolescentes.

Keypoints

What is known
- ARFID, recognized in DSM-5 and ICD-11, details a condition where individuals exhibit limited food intake, impacting nutritional and psychosocial well-being.
- Unlike traditional eating disorders, ARFID lacks body image concerns, emphasizing the need for unique approaches to diagnosis and treatment.
- The prevalence of ARFID varies widely, with existing studies indicating a need for better screening tools and standardized diagnostic criteria.

What is added
- ARFID's association with gastrointestinal, neurological, and psychiatric comorbidities underscores the necessity for early, comprehensive interventions.
- The complexity of ARFID, coupled with its significant comorbidities, demands a multidisciplinary treatment approach and increased awareness among healthcare providers.
- Future research on ARFID should focus on elucidating its etiology, improving diagnostic tools, and developing effective, holistic treatment strategies.

Introduction

Avoidant/Restrictive Food Intake Disorder (ARFID) is a diagnosis introduced in the DSM-5[1] in 2013 and recognized by the ICD-11[2] in 2019, highlighting its acceptance in the global psychiatric community. ARFID outlines a condition where individuals exhibit a significant limitation in food intake, due to a lack of interest in food, fear of aversive consequences, or sensory sensitivities. This disorder extends beyond the limitations set by the DSM-IV, recognizing affected individuals across all age groups, not confined to early childhood. The implications of ARFID are profound, leading to nutritional deficiencies, weight loss, and notable psychosocial difficulties, setting it apart from other eating disorders which typically involve concerns over body image or an explicit desire to lose weight[1].

The epidemiology of ARFID, although increasingly studied, remains inadequately characterized, with reported prevalence rates showing wide variation, ranging from 0.3% to 15.5% in a non-clinical sample and from 5% to 64% in specialized pediatric eating disorder department samples[3]. This variability underscores the urgent need for comprehensive epidemiological studies using standardized diagnostic criteria and assessment tools to better define the disorder's scope and impact[3,4].

The treatment of ARFID demands a comprehensive, multidisciplinary approach that integrates psychological therapies, nutritional guidance and, when necessary, pharmacological support to address the multifaceted nature of the disorder. Effective management often requires customized interventions that consider the unique motivations behind food avoidance for each individual[5-7].

Comorbid conditions are commonly observed with ARFID, including anxiety disorders, obsessive-compulsive disorder (OCD) and various neurodevelopmental disorders[1]. These comorbidities complicate the clinical picture, necessitating an integrated treatment plan that addresses both ARFID and its psychiatric or developmental co-occurrences.

The purpose of this systematic literature review is to synthesize what is already known about the most common comorbidities of ARFID, whilst focusing on children and adolescents. Accurate knowledge of comorbidities is crucial for effective clinical management, treatment planning, and resource allocation. It informs public health strategies, influences research design, and contributes to patient-centered care by recognizing the interconnected nature of health conditions. Overall, understanding comorbidities is essential for improving patient outcomes and optimizing healthcare systems. This knowledge will enable a more comprehensive understanding of the topic, effectively supporting clinical practice and shaping preventive strategies and interventions.

Methods

This systematic review of literature was developed in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[8].

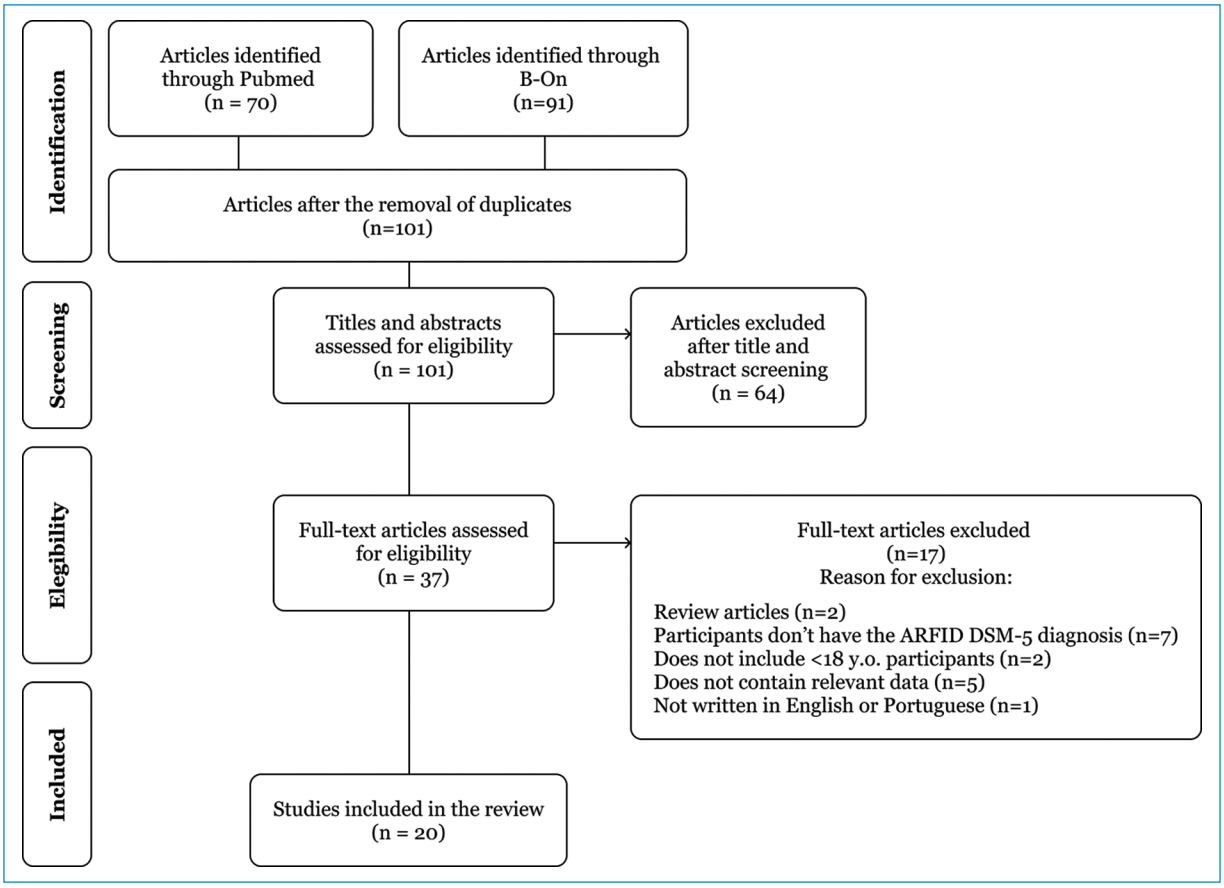

Figure 1. Flow chart of reviewed studies, according to PRISMA[8].

The first search was conducted in July 2023 and the final search was on the 5th of September, 2023.

Two databases were used: Pubmed and B-On - a Portuguese platform, sponsored by the Foundation for Science and Technology - that gives open access to several databases such as Medline, Elsevier and Web of Science.

Articles published between January 2013 and September 2023 were identified. ARFID was introduced as a diagnosis in the DSM-5, published in 2013. Consequently, 2013 was the starting point for the search.

Using the keywords "Avoidant/Restrictive Food Intake Disorder", "Comorbidities", "Child", and "Adolescent", 70 articles were identified in Pubmed and 91 in B-On. After removing duplicates, 101 abstracts were screened and 37 articles remained for full assessment. Applying the inclusion criteria, a total of 20 articles met the requirements and were selected for the final systematic review[9-28].

The review selection process is summarized in the PRISMA flow chart in figure 1.

The review was registered with the international prospective register of systematic reviews (PROSPERO) (PROSPERO CRD42024503067).

Inclusion criteria

- Studies published between 1 January 2013 and 5 September 2023;
- Studies written in Portuguese or English;
- Studies with a mean age of participants below or equal to 18 years old;
- Studies with participants diagnosed with ARFID according to DSM-5 or ICD-11 criteria;
- Studies containing relevant data on the participants' medical or psychiatric comorbidities.

Exclusion criteria

- Studies published before January 2013 and after September 2023;
- Study design: case studies, qualitative studies, letters to the editor, reviews (literature reviews, systematic reviews, and meta-analyses), comments, or manuscripts;
- Studies with a mean age of participants above 18 years old.

Data extraction

Data was extracted from each article as regards the author, country, year of publication, design and method, sample size, gender and age of participants, diagnostic criteria, description of participants, setting of the study, medical comorbidities, and psychiatric comorbidities. Other relevant data was also collected, such as signs of medical instability, family history of psychiatric disorders, criteria A symptoms according to the DSM-5, presence of infection prior to the onset of the eating disorder (ED), trigger for the ED, demonstration of somatic concerns by the participants, and comparisons between different phenotypes.

Quality assessment

The risk of bias was assessed with the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool. This tool assesses, for each study, the risk of bias in seven different domains: confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of reported results. Each domain, as well as the overall risk of bias, is categorized using a traffic light color code: green for low risk, yellow for moderate risk, and red for high risk. Additionally, a question mark indicates that the data for a particular domain was not adequately reported or was unclear (Figs. 1 and 3)[29-31].

Results

Twenty articles were reviewed, with a total of 1178 participants. The selected studies included children and adolescents with a mean age inferior or equal to 18 years old (the maximum age reported was 23 years old), diagnosed with ARFID, using DSM-5 or ICD-11 criteria.

Key aspects of the included studies are presented in tables 1 and 2.

Characteristics of the included studies

The majority were conducted in North America (n = 10) (United States of America (USA) (n = 5)[9,13,15,18,26] and Canada (n = 5))[11,12,23,27,28] and four were carried out in multiple countries[10,20,22,24]. Two studies took place in Japan[16,25] and four in Europe: United Kingdom[17], Italy[14], Spain[19], and Germany[21].

All of the included studies focused on clinical populations, with most drawing on samples from pediatric eating disorder specialized departments (n = 11)[9-15,17,19,23,27] and utilizing retrospective chart reviews (n = 11)[10-15,16,18,23,26,27]. ARFID diagnosis was established using the DSM-5 or ICD-11 criteria.

Quality assessment

The risk of bias, assessed with the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool, is depicted across multiple studies in figure 2, which utilizes a traffic light color code to evaluate individual studies across seven domains of bias and an overall appreciation. Figure 3 summarizes this data in a bar chart, quantitatively presenting the overall proportion of studies falling into low, moderate, or unknown risk categories for each bias domain[29-31].

Results from the included studies: medical comorbidities

From the 20 selected studies, eight provided data on medical comorbidities, giving a total sample of 383 ARFID patients who were assessed for these comorbid conditions[9,10,13,21-23,26,28]. However, only 353 observations of comorbidities were recorded. Due to the consistent methodology employed across the studies, the results were aggregated to provide a more robust body of evidence (Fig. 4).

All eight studies focus on gastrointestinal (GI) symptoms or conditions, showing that about 38% of the observations include a related complaint or disease. Among these observations, there were 117 instances reporting GI symptoms. Of these, 56 mentioned specific issues such as diarrhea, gastroesophageal reflux, early satiety, nausea, gastroparesis, or abdominal pain, while 61 did not specify the symptoms. Additionally, 14 observations involved a GI disease diagnosis, with seven cases of either chronic abdominal pain or inflammatory conditions and seven not specifying the disease.

Secondly, 25% of the observations indicate a neurological-associated condition. Sensory problems were reported 23 times among the patients. There were 18 instances mentioning migraines and cognitive impairment was reported 17 times. Fifteen observations registered episodes of dizziness, four reported chronic pain, three a diagnosis of brain palsy, and two a history of seizures. One observation did not specify a condition.

The immune system was affected in 10% of the observations. Allergies to food and drugs were reported in 19 and six instances, respectively. Asthma was documented in nine observations and atopic dermatitis in one.

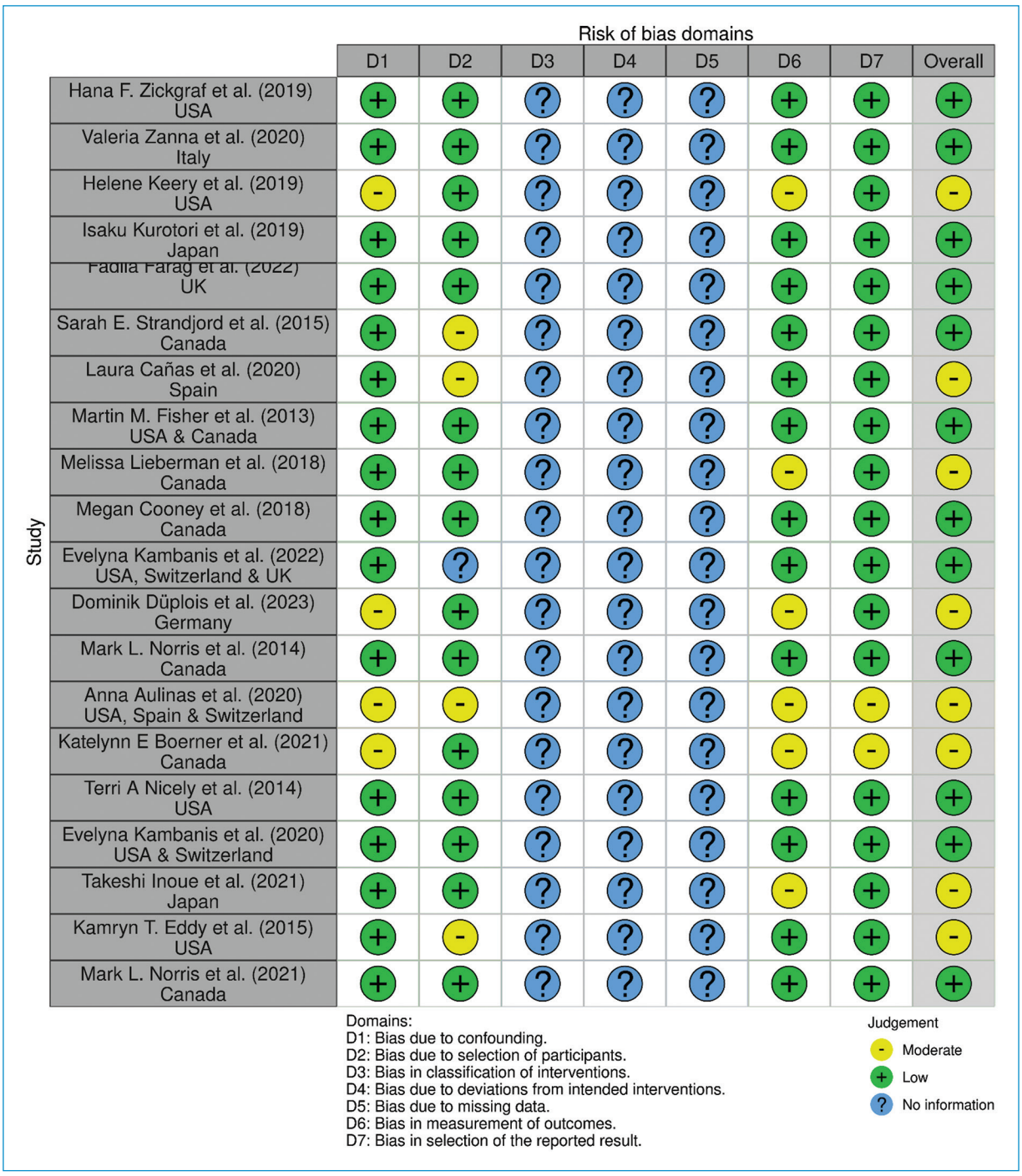

Figure 2. Traffic-light plot with the risk of bias domains assessment for each study, using the ROBINS-I tool[29,31].

Five observations indicated endocrine conditions, three a congenital anomaly, and another three a musculoskeletal problem. One instance referred to an oncological problem, one Lyme disease, and one interstitial cystitis. Lastly, 12 reported pain of some kind, 18 did not specify the symptoms, and 50 referred to an unspecified medical condition.

Results from the included studies: psychiatric comorbidities

All but two studies reported psychiatric comorbidities, giving a total sample of 1125 participants analyzed for psychiatric comorbidities[9-21,23-25,27,28]. However, only 924 observations of comorbidities were recorded.

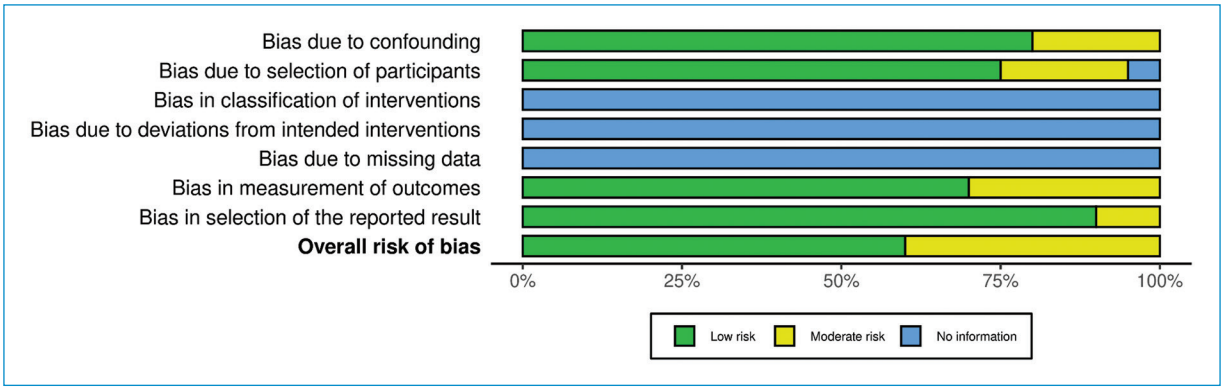

Figure 3. Bar chart with quantitative summary of the risk of bias domains assessment, using the ROBINS-I tool[29,31].

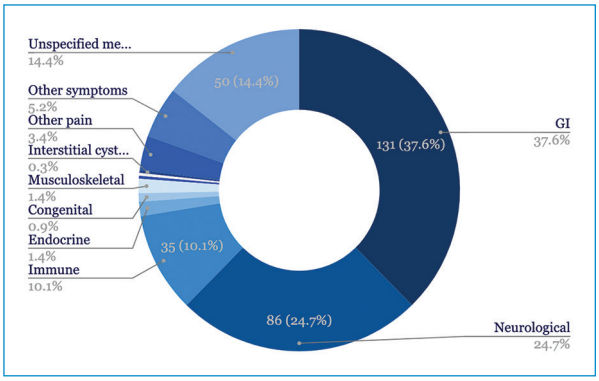

Figure 4. Pie chart depicting the most prevalent medical comorbidities.

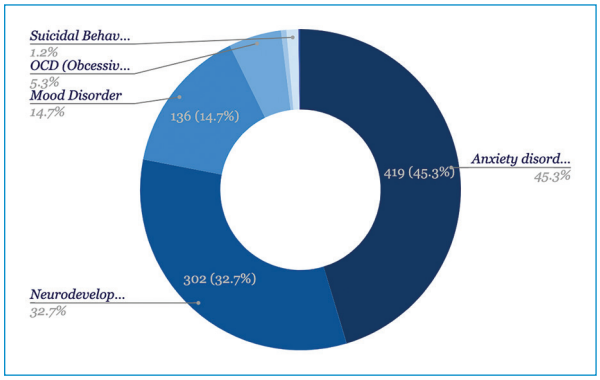

Figure 5. Pie chart depicting the most prevalent psychiatric comorbidities.

Due to the consistent methodology employed across the studies, the results were aggregated to provide a more robust body of evidence (Fig. 5).

From this instance pool, 45% of the observations recorded anxiety disorders, more specifically, 88 instances of generalized anxiety disorder (GAD), 19 a specific phobia, 14 social anxiety disorder, with the same number reporting panic disorder, four post-traumatic stress disorder (PTSD) and 280 an unspecified anxiety disorder.

Secondly, neurodevelopmental disorders were reported in 33% of observations. Autistic spectrum disorder (ASD) was diagnosed in 179 instances, attention deficit hyperactivity disorder (ADHD) in 68, a learning disability in 15, and 40 reported an unspecified neurodevelopmental disorder.

Mood disorders were found in 15% of the observations. Twenty-nine instances presented a depressive disorder or dysthymia, 23 with major depressive disorder (MDD), and 84 did not specify.

Lastly, 5% of the observations mentioned a co-occurring diagnosis of OCD, there were 11 instances of suicidal behavior, five of a conduct disorder, one a dissociative disorder, and ten of an unspecified psychiatric disorder.

Additionally, three studies reported a psychiatric history[15,22,24], four a family's psychiatric and eating disorder history[11,16,18,22], two the use of psychiatric medication[15,22], one showed data on a history of abuse, self-harm, and substance use[23], and one evaluated the distribution of psychiatric comorbidities in the different ARFID phenotypes[27].

Results from the included studies: other findings

In this section, other relevant data that was found through the analysis of the studies is presented.

Three studies reported criteria A from the DSM-5 diagnostic criteria, showing the frequency of each one

Table 1. Characteristics of the included studies

Author, year, and country	Design	Method	Sample description	Sample setting	Sample size	Sample gender	Sample age	How was the ARFID diagnosis made?
Hana F. Zickgraf et al. (2019) USA[9]	Retrospective chart review	Data collected either prospectively since 2013 or retrospectively from 2008 to 2012, from participants	Patients admitted to a Partial Hospitalization Program (PHP) and diagnosed with Avoidant/Restrictive Food Intake Disorder (ARFID)	Pediatric eating disorder Partial Hospitalization Program	n = 83	♂n = 19 ♀n = 64	8-17 (mean of 11.4 y. o.)	Using a checklist of DSM-5 eating disorder symptoms
Valeria Zanna et al. (2020) Italy[14]	Retrospective chart review	Retrospective chart review of patients under the age of 18 who received specific ED diagnoses by the DSM-IV criteria, between January 2010 and September 2017, which were later reclassified as DSM-5 criteria by an expert	Participants were children and adolescents under 18 years old, initially diagnosed according to DSM-IV criteria with Anorexia Nervosa (AN), Feeding Disorder of Infancy or Early Childhood, or Eating Disorder Not Otherwise Specified. Diagnosis later reclassified as ARFID according to DSM-5 criteria by an expert	Pediatric tertiary care ED program	n = 94	♂n = 36 ♀n = 58	mean age < 18 y. o.	Using a checklist of DSM-5 eating disorder symptoms
Helene Keery et al. (2019) USA[15]	Longitudinal study	Data collection was done through interviews, pen-and-paper assessments, and electronic health records	Patients aged 7-19 years old who were diagnosed with a DSM-5 feeding or eating disorder and agreed to participate in outpatient treatment at Children's Minnesota Hospital, between July 2015 and December 2017	Center for the Treatment of Eating Disorders (CTED)	n = 106	♂n = 43 ♀n = 63	7-19	DSM-5 criteria
Isaku Kurotori et al. (2019) Japan[16]	Observational study	Retrospective chart review	Pediatric patients diagnosed with eating disorders, requiring hospitalization due to their medically unstable state	Child and adolescent psychiatric ward in a pediatric hospital	n = 13	♂n = 2 ♀n = 11	7-14 (mean of 10.7 y. o.)	DSM-5 criteria
Fadila Farag et al. (2022) UK[17]	Cross-sectional	Data collected prospectively from patients seen by the tertiary feeding department	Pediatric patients experiencing severe feeding difficulties referred to tertiary feeding clinic at Evelina London Children's Hospital between January 2013 and June 2019	Tertiary care pediatric feeding clinic	n = 263	♂n = 215 ♀n = 48	1-20 (mean of 6.8 y. o.)	DSM-5 criteria
Sarah E. Strandjord et al. (2015) Canada[18]	Retrospective chart review	Data was collected by reviewing medical records	Patients who were hospitalized for refeeding and met DSM-5 criteria for an eating disorder, at an academic medical center between 2008 and 2014	Academic medical center	n = 41	♂n = 6 ♀n = 35	14-18 (mean of 16.0 y. o.)	DSM-5 criteria

(Continues)

Table 1. Characteristics of the included studies *(continued)*

Author, year, and country	Design	Method	Sample description	Sample setting	Sample size	Sample gender	Sample age	How was the ARFID diagnosis made?
Laura Cañas et al. (2020) Spain[19]	Descriptive observational and comparative study	Data collection was conducted through assessments of children and adolescents, along with their families, within a 15-day period starting from their first visit to the eating disorders unit of Hospital Sant Joan de Déu in Barcelona	Eating disorder patients seeking treatment from October 2015 to May 2018 at the eating disorders unit of Hospital Sant Joan de Déu in Barcelona, Spain	Eating disorders unit	n = 33 (outpatients n = 29, partial	♂n = 20 ♀n = 13	7-17 (mean of 10.8 y. o.)	DSM-5 criteria
Martin M. Fisher et al. (2013) USA & Canada[10]	Cross-sectional	Retrospective chart review	New patients who presented to seven adolescent medicine eating disorder programs in the US and Canada between January and December 2010	Adolescent medicine-based ED programs	n = 98	♂n = 28 ♀n = 70	8-18 (mean of 12.9 y. o.)	DSM-5 criteria
Melissa Lieberman et al. (2018) Canada[28]	Observational study	Data was collected through clinical interviews, psychometric questionnaires, and chart reviews	In- and outpatients who met the DSM-5 criteria for AN and ARFID, between May 2013 and January 2017, that were part of the specialized COPE program at the Hospital for Sick Children in Toronto	Specialized program for children under 13 years of age	n = 29	♂n = 7 ♀n = 22	8-13 (mean of 10.8 y. o.)	DSM-5 criteria
Megan Cooney et al. (2018) Canada[12]	Cross-sectional	Retrospective chart review	Patients referred for a comprehensive eating disorder assessment at a tertiary care pediatric hospital between May 2013 and April 2016	Pediatric tertiary care ED program	n = 28	♂n = 10 ♀n = 18	9-18 (mean of 13.2 y. o.)	DSM-5 criteria
Evelyna Kambanis et al. (2022) USA, Switzerland & UK[20]	Comparative observational study	Data was collected through structured interviews	Female participants diagnosed with ED; part of larger studies on the neurobiology of eating disorders	Within the context of broader research projects at an academic institution, focusing on the neurobiology of eating disorders	n = 51	♂n = 0 ♀n = 51	10-23 (mean of 16.6 y. o.)	DSM-5 criteria
Dominik Düplois et al. (2023) Germany[21]	Comparative observational study	Data was collected with semi-structured clinical interviews	Patients seeking in- or outpatient treatment for a restrictive feeding or eating disorder, at Leipzig University Medical Center between February 2018 and October 2021	Leipzig University Medical Center	n = 19	♂n = 7 ♀n = 12	0-17 (mean of 10.6 y. o.)	DSM-5 criteria

(Continues)

Table 1. Characteristics of the included studies *(continued)*

Author, year, and country	Design	Method	Sample description	Sample setting	Sample size	Sample gender	Sample age	How was the ARFID diagnosis made?
Mark L. Norris et al. (2014) Canada[11]	Cross-sectional	Retrospective chart review of patients diagnosed with food avoidant emotional disorder, childhood AN, selective eating, eating disorder not otherwise specified (EDNOS), or EDNOS restrictive subtype, or those that were discharged without diagnosis	Patients who received an ED initial assessment between 2000 and 2011	Pediatric ED treatment program	n = 34	♂n = 7 ♀n = 27	(mean of 13.7 y. o.)	DSM-5 criteria
Anna Aulinas et al. (2021) USA, Spain & Switzerland[22]	Cross-sectional	Data was collected from studies investigating the neurobiology of restrictive EDs	Low-weight females diagnosed with an ED	Pediatric Endocrinology Unit	n = 20	♂n = 0 ♀n = 20	10-22 (mean of 14.3 y. o.)	No reference
Katelynn E Boerner et al. (2021) Canada[23]	Retrospective chart review	Data was collected through a retrospective review of medical records	Patients diagnosed with ARFID or a GI-related Somatic Symptom and Related Disorder (SSRD), between January 2014 and January 2019	Specialized ED program	n = 62	♂n = 19 ♀n = 43	5-18 (mean of 14.0 y. o.)	No reference
Terri A Nicely et al. (2014) USA[13]	Cross-sectional	Retrospective chart review	Patients admitted to a day program for children and adolescents with EDs between August 2008 and May 2012	Day program for EDs	n = 39	♂n = 8 ♀n = 31	7-17 (mean of 11.1 y. o.)	DSM-5 criteria
Evelyna Kambanis et al. (2019) USA & Switzerland[24]	Cross-sectional	Data was collected through structured interviews	Children and adolescents with full and subthreshold ARFID	Within the context of broader research projects at an academic institution, focusing on the neurobiology of eating disorders	n = 74	♂n = 38 ♀n = 36	9-22 (mean of 15.0 y. o.)	DSM-5 criteria
Takeshi Inoue et al. (2021) Japan[25]	Cross-sectional	Multicenter cohort study	Children with Feeding and Eating Disorders (FEDs) recruited as part of the Japanese Pediatric EDs Outcome: a Prospective Multicenter Cohort Study (J-PED) study	Multiple medical institutions throughout Japan	n = 32	♂n = 7 ♀n = 25	5-15 (mean of 11.8 y. o.)	No reference
Kamryn T. Eddy et al. (2015) USA[26]	Cross-sectional	Retrospective chart review	Patients who presented for an initial evaluation at one of the 19 Boston area pediatric gastroenterology clinics affiliated with Massachusetts General Hospital, comprising a teaching hospital and community settings, between January 2008 and December 2008	Pediatric gastroenterology clinics	n = 33	♂n = 22 ♀n = 11	8-18 (mean of 11.4 y. o.)	DSM-5 criteria
Mark L. Norris et al. (2021) Canada[27]	Longitudinal study	Retrospective chart review	Patients meeting criteria for ARFID who were admitted to a specialized pilot clinic within a tertiary care children's hospital in Ontario, from December 2014 to June 2016	Specialized pilot clinic	n = 26	♂n = 10 ♀n = 16	9-18 (mean of 13.9 y. o.)	DSM-5 criteria

ARFID: Avoidant/Restrictive Food Intake Disorder; ED: eating disorder; AN: Anorexia Nervosa; EDNOS: eating disorder not otherwise specified; GI: gastrointestinal.

Table 2. Results from the included studies

Author, year, and country	Medical comorbidities	Psychiatric comorbidities	Other findings
Hana F. Zickgraf et al. (2019) USA[9]	Gastrointestinal (GI) symptoms (gastroesophageal reflux, early satiety, nausea, gastroparesis, and abdominal pain) n = 26 (31.3%) Asthma n = 4 Cerebral palsy/ambulatory dysfunction n = 3 Amplified musculoskeletal pain syndrome n = 2 Seizure history n = 2 Eczema n = 1 Juvenile rheumatoid arthritis n = 1 Lyme disease n = 1 Ehlers-Danlos syndrome n = 1 Tetralogy of Fallot n = 1 Interstitial cystitis n = 1 Scoliosis n = 1	Anxiety disorder n = 61 Mood disorder n = 17 Obsessive-compulsive disorder (OCD) n = 17 Attention-deficit/hyperactivity disorder (ADHD) n = 10 Developmental delay n = 6	The criteria A symptoms of DSM-5 A1 (weight loss) n = 67 A1 (faltering growth) n = 11 A2 (nutritional deficiency) n = 78 A3 (dependence on supplements) n = 28
Valeria Zanna et al. (2020) Italy[14]	No reference	Anxiety disorder n = 33 Mood disorder n = 15	
Helene Keery et al. (2019) USA[15]	No reference	Anxiety disorder n = 61 (57.5%) ADHD n = 25 (23.6%) Depressive disorder n = 20 (18.9%) Autistic spectrum disorder (ASD) n = 6 (5.7%) History of eating disorders n = 40 Use of psychotropic medication n = 38	Signs of medical instability: Orthostatic instability, (> 20 beats per minute (bpm), > 10 mmHg) n = 57 (53.8%) Amenorrhea n = 7 (11.1%) Bradycardia (< 50 bpm) n = 5 (4.7%) Hypotension (systolic pressure < 90 mmHg) n = 2 (1.9%)
Isaku Kurotori et al. (2019) Japan[16]	No reference	Developmental disorders n = 6	Family history of mental disorders n = 6
Fadila Farag et al. (2022) UK[17]	No reference	ASD n = 144	
Sarah E. Strandjord et al. (2015) Canada[18]	No reference	Unspecified psychiatric comorbidity n = 5	Family history: Eating disorder n = 3 Other psychiatric disorder n = 9
Laura Cañas et al. (2020) Spain[19]	No reference	Anxiety disorders n = 16 (59.3%) ADHD n = 7 (25.9%) OCD n = 2 (7.4%) Behavioral disorders n = 2 (7.4%) Depressive disorders n = 0 (0.0%)	The criteria A symptoms of DSM-5: A1 (significant weight loss or faltering growth) n = 20 A2 (significant nutritional deficiency) n = 24 A3 (dependence on oral nutritional supplements) n = 12 A4 (marked interference with psychosocial functioning) n = 16
Martin M. Fisher et al. (2013) USA & Canada[10]	Unspecified medical condition related to the disorder n = 34 unrelated to the disorder n = 16 *mentions that patients had GI symptoms and food allergies but does not have any specific numbers/data	Anxiety disorder: Generalized anxiety disorder (GAD) n = 28 Other n = 23 Mood disorder: Major depressive disorder (MDD)/ Dysthymia n = 7 Other n = 11 OCD n = 6	

(Continues)

Table 2. Results from the included studies *(continued)*

Author, year, and country	Medical comorbidities	Psychiatric comorbidities	Other findings
Melissa Lieberman et al. (2018) Canada[28]	Food allergies n = 4 Abdominal pain n = 9	GAD n = 7 OCD n = 6 Unspecified neurodevelopmental disorder n = 3 ADHD n = 1 ASD n = 1 Mood disorder n = 1 Other specified dissociative disorder (OSDD) n = 1	Infection prior to onset of ED n = 32 (37.9%)
Megan Cooney et al. (2018) Canada[12]	No reference	Anxiety disorder n = 10 ADHD n = 4 MDD n = 2 Other unspecified psychiatric comorbidity n = 5	The criteria A symptoms of DSM-5: A1 (significant weight loss or faltering growth) n = 27 A2 (significant nutritional deficiency) n = 0 A3 (dependence on oral nutritional supplements) n = 1 A4 (marked interference with psychosocial functioning) n = 0 Trigger for their eating disturbance: Abdominal pain n = 5 Bullying n = 3 Death of a family member/ friend n = 2 Starting a medication n = 2 Having emesis n = 2 or witnessing emesis n = 1 Concern for food allergy n = 2 Concern for animal rights n = 1
Evelyna Kambanis et al. (2022) USA, Switzerland & UK[20]	No reference	GAD n = 18 (35.0%) MDD n = 15 (29.0%) Panic disorder n = 7 (14.0%) Specific phobia n = 5 (10.0%) Social anxiety disorder n = 5 (10.0%) Suicidality n = 5 (10.0%) ADHD n = 4 (8.0%) Post-traumatic stress disorder (PTSD) n = 4 (8.0%) Other specified depressive disorder n = 3 (6.0%) OCD n = 3 (6.0%) Other specified ADHD n = 2 (4.0%) Other specified anxiety disorder n = 1 (2.0%) ASD n = 1 (2.0%) Persistent depressive disorder n = 1 (2.0%) Separation anxiety disorder n = 0 (0.0%)	
Dominik Düplois et al. (2023) Germany[21]	GI diseases n = 7 (36.8%) Metabolic disorders n = 3 (15.8%) Congenital anomalies n = 2 (10.5%)	Affective disorders n = 8 (42.1%) ADHD n = 2 (10.5%) OCD n = 1 (5.3%)	
Mark L. Norris et al. (2014) Canada[11]	No reference	GAD n = 17 MDD n = 4 *other diagnoses including panic disorder, OCD, and social phobia were present but there was no mention of values	Immediate family member with a diagnosed psychiatric disorder n = 5

(Continues)

Table 2. Results from the included studies *(continued)*

Author, year, and country	Medical comorbidities	Psychiatric comorbidities	Other findings
Anna Aulinas et al. (2021) USA, Spain & Switzerland[22]	Gastrointestinal system: History of GI symptoms n = 9 (45.0%) Acid reflux n = 8 (40.0%) Delayed gastric emptying n = 2 (10.0%) Irritable bowel syndrome n = 1 (5.0%) Immune system: Drug allergies n = 6 (30.0%) Asthma n = 5 (25.0%) Food allergies n = 4 (20.0%)	History of depression n = 3 History of anxiety n = 13 History of OCD n = 0 Current psychiatric medication: Total n = 12 (60.0%) Antidepressants n = 5 (25.0%) Anxiolytics n = 3 (15.0%) Psychostimulants n = 3 (15.0%) Antihistamines n = 3 (15.0%)	Family history of eating disorders n = 2 Family history of psychiatric disorders n = 9
Katelynn E Boerner et al. (2021) Canada[23]	Co-occurring medical diagnosis: Total n = 14 (22.6%) GI conditions (chronic abdominal pain and inflammatory conditions) n = 6 (9.7%) Chronic (non-abdominal) pain n = 2 (3.2%) Endocrine conditions n = 2 (3.2%) Neurological conditions n = 1 (1.6%) Oncological conditions n = 1 (1.6%) Physical symptoms (reported at assessment) Total n = 58 (93.5%) GI n = 52 (83.9%) Headache n = 21 (33.9%) Cognitive problems n = 17 (27.4%) Dizziness or fainting/syncope n = 15 (24.2%) Sensory problems n = 8 (12.9%) Perceptual disturbances n = 3 (4.8%) Movement problems n = 2 (3.2%) Other pain n = 12 (19.4%) Other symptoms n = 18 (29.0%)	Co-occurring psychiatric diagnosis: Total n = 33 (53.2%) Anxiety disorder n = 27 (43.5%) Neurodevelopmental disorder n = 8 (12.9%) OCD n = 7 (11.3%) Bipolar-related or depressive disorder n = 6 (9.7%) Disruptive, impulse-control, or conduct disorder n = 1 (1.6%) History of abuse Physical n = 4 (6.5%) Sexual n = 1 (1.6%) Self-harm and suicidality History of suicidal ideation n = 17 (27.4%) History of self-harm n = 8 (12.9%) History of suicide attempt n = 4 (6.5%) Substance use (historical and/or current): Total n = 8 (12.9%) Alcohol use n = 8 (12.9%) Illicit substance use n = 6 (9.7%) Prescription medication misuse n = 2 (3.2%)	This study compared characteristics of pediatric patients diagnosed with ARFID to those with GI-related SSRD. 16% of the total sample reported symptoms consistent with co-occurring diagnoses of ARFID and SSRD
Terri A Nicely et al. (2014) USA[13]	Symptoms and features Fear of choking or vomiting n = 17 (47.0%) Enteral supplement use n = 18 (46.0%) Recent medical specialist consult n = 18 (46.0%) Sensory issues n = 10 (26.0%) Food allergy n = 8 (20.0%) Excessive exercise n = 6 (15.0%) Purge-vomit n = 0 (0.0%)	Psychiatric comorbidities Anxiety disorder n = 28 (72.0%) Mood disorder n = 13 (33.0%) Cognitive impairment n = 10 (26.0%) ASD n = 5 (13.0%) Learning disorder n = 4 (10.0%) ADHD n = 2 (4.0%)	21% of participants exhibited body preoccupation with somatic concerns. For example, some children were fixated on fears of physical illness due to issues related to shape/weight, e.g., high cholesterol and/or obesity leading to heart disease, either because of personal experiences with relatives or information in their school curriculum
Evelyna Kambanis et al. (2019) USA & Switzerland[24]	No reference	Anxiety, OCD, and trauma-related disorders: Total: current (C) n = 26 (35.0%)/ lifetime (L) n = 30 (41.0%) GAD: C n = 18 (24.0%)/L n = 18 (24.0%) Panic disorder: C n = 7 (10.0%)/L n = 9 (12.0%) Social anxiety disorder: C n = 7 (10.0%)/L n = 9 (12.0%) Specific phobia: C n = 5 (7.0%)/L n = 5 (7.0%)	The sensory sensitivity profile (rated on a 0 – 6 scale) was associated with more than twice the odds of a current or lifetime comorbid neurodevelopmental, disruptive, or conduct disorder; The fear of aversive consequences profile was associated with more than twice the odds of a current

(Continues)

Table 2. Results from the included studies *(continued)*

Author, year, and country	Medical comorbidities	Psychiatric comorbidities	Other findings
		OCD: C n = 3 (4.0%)/L n = 3 (4.0%) Agoraphobia: C n = 1 (1.0%)/L n = 1 (1.0%) Separation anxiety disorder: C n = 0 (0.0%)/L n = 1 (1.0%) Other specified anxiety disorder: C n = 1 (1.0%)/L n = 1 (1.0%) PTSD: C n = 0 (0.0%)/L n = 1 (1.0%) Neurodevelopmental, disruptive, and conduct disorders: Total: C n = 12 (16.0%)/L n = 14 (19.0%) ADHD: C n = 6 (8.0%)/L n = 7 (10.0%) Other specified ADHD: C n = 5 (7.0%)/L n = 5 (7.0%) Oppositional defiant disorder: C n = 2 (3.0%)/L n = 2 (3.0%) ASD: C n = 2 (3.0%)/L n = 2 (3.0%) Suicidality: Total: C n = 6 (8.0%)/L n = 10 (14.0%) Depressive and bipolar-related disorders: Total: C n = 3 (4.0%)/L n = 15 (20.0%): MDD: C n = 2 (3.0%)/L n = 10 (14.0%) Other specified depressive disorder: C n = 1 (1.0%)/L n = 3 (4.0%) Persistent depressive disorder: C n = 0 (0.0%)/L n = 2 (3.0%) Eating disorders and substance-related disorders: Total: C n = 0 (0.0%)/L n = 1 (1.0%) Binge eating disorder: C n = 0 (0.0%)/L n = 1 (1.0%) Schizophrenia spectrum and other psychotic disorders: Total: C n = 0 (0.0%)/L n = 0 (0.0%)	comorbid anxiety, OCD, or trauma-related disorder; The ARFID sensory sensitivity profile was associated with nearly three times the odds of a current or lifetime comorbid anxiety, OCD, or trauma-related disorder; The sensory sensitivity profile was associated with more than twice the odds of a lifetime comorbid depressive or bipolar-related disorder; Severity in the sensory sensitivity profile contributed to both current and lifetime likelihood of neurodevelopmental, disruptive, and conduct disorders; and severity in the fear of aversive consequences profile contributed to current and lifetime anxiety, OCD, and trauma-related disorders
Takeshi Inoue et al. (2021) Japan[25]	No reference	ASD n = 4 (12.5%)	
Kamryn T. Eddy et al. (2015) USA[26]	Presenting GI complaint: Poor weight gain/growth n = 17 Low weight/underweight n = 10 Poor appetite n = 10 Abdominal pain n = 9 Weight loss n = 5 Reflux n = 5 Nausea n = 3 Diarrhea/loose stools n = 3 Food allergies n = 3	No reference	
Mark L. Norris et al. (2021) Canada[27]	No reference	Anxiety disorder: ARFID total n = 19 (73.1%) Aversive n = 6 (100.0%) Sensory n = 2 (100.0%) Low appetite, limited interest n = 4 (50.0%) ARFID-Mixed n = 7 (70.0%) ASD: ARFID total n = 16 (23.1%)	Patients with aversive presentations presented an abbreviated course of illnesses and were all diagnosed with anxiety. Patients with low appetite represented the highest proportion of single-symptom presentations

(Continues)

Table 2. Results from the included studies *(continued)*

Author, year, and country	Medical comorbidities	Psychiatric comorbidities	Other findings
		Aversive n = 1 (16.7%) Sensory n = 1 (50.0%) Low appetite, limited interest n = 0 (0.0%) ARFID-Mixed n = 4 (40.0%) Mood disorder: ARFID total n = 9 (34.60%) Aversive n = 3 (50.0%) Sensory n = 1 (50.0%) Low appetite, limited interest n = 2 (25.0%) ARFID-Mixed n = 3 (30.0%) Learning difficulties: ARFID total n = 8 (30.08%) Aversive n = 1 (16.7%) Sensory n = 0 (0.0%) Low appetite, limited interest n = 3 (37.5%) ARFID-Mixed n = 4 (40.0%) ADHD: ARFID total n = 6 (23.1%) Aversive n = 2 (33.3%) Sensory n = 1 (50.0%) Low appetite, limited interest n = 0 (0.0%) ARFID-Mixed n = 3 (30.0%) OCD: ARFID total n = 4 (15.4%) Aversive n = 2 (33.3%) Sensory n = 0 (0.0%) Low appetite, limited interest n = 0 (0.0%) ARFID-Mixed n = 2 (20.0%)	Patients with sensory-based food avoidance (i.e., extremely selective eaters) are less likely to present with markers of medical instability, and as such, would have been less likely to meet inclusion criteria for this pilot initiative

GI: gastrointestinal; OCD: obsessive-compulsive disorder; ADHD: attention-deficit/hyperactivity disorder; ASD: autistic spectrum disorder; GAD: generalized anxiety disorder; MDD: major depressive disorder; OSDD: other specified dissociative disorder; PTSD: post-traumatic stress disorder; ARFID: avoidant/restrictive food intake disorder; SSRD: somatic symptom and related disorder.

in their sample[9,12,19]. Due to the consistent methodology employed across the studies, the results were aggregated to provide a more robust body of evidence. The sample consisted of 144 participants, of whom 125 filled the A1 criteria (significant weight loss (or failure to achieve expected weight gain or faltering growth in children)), 102 the A2 criteria (significant nutritional deficiency), 41 the A3 criteria (dependence on enteral feeding or oral nutritional supplements), and 16 the A4 criteria (marked interference with psychosocial functioning).

Keery et al. reported signs of medical instability such as bradycardia, hypotension, orthostatic instability, and amenorrhea[15].

While Lieberman et al. found that some participants had an infection before the onset of the eating disorder, Cooney et al. investigated what the trigger for the eating disorder was in each participant (Table 2)[12,28].

Another interesting finding, according to Nicely et al., was that although individuals with ARFID do not have body distortion (as seen in anorexia nervosa), 21% of the participants from that study had a fear of physical illness[13].

Lastly, Kambanis et al. and Norris et al. presented some noteworthy conclusions when it comes to the different ARFID presentations[24,27]. Participants with a lack of interest in food are more likely to present one single symptom. Participants with an aversive phenotype have a shorter course of illness and are twice as likely as the other phenotypes to have comorbid anxiety, OCD, and trauma-related disorder. Participants with sensory sensitivity are three times as likely as the other phenotypes to have comorbid anxiety, OCD, and trauma-related disorder, and twice as likely as the other phenotypes to have comorbid mood, neurodevelopmental, and conduct disorders. However, this last phenotype is less likely to present with signs of medical instability.

Discussion

To our understanding, this is the first systematic literature review that specifically targets the most prevalent comorbidities in children and adolescents diagnosed with ARFID. Knowledge about comorbid conditions is fundamental to improving healthcare outcomes, as it shapes effective treatment, prognosis, and patient care. The findings from this review indicate that there are a significant number of comorbidities amongst young individuals with ARFID[10,19,21,28]. This is congruent with other literature that finds a greater medical and psychiatric comorbidity in this population, in comparison with other EDs[19].

When it comes to medical comorbidities, GI, neurological, and immune disorders are the most frequent. The high prevalence of GI symptoms and conditions among the participants suggests a connection between ARFID and digestive health, such as central sensitization and altered gut physiology, and also raises questions about the etiology of this disorder[23]. GI problems can cause discomfort during eating, potentially influencing food avoidance or restrictive behaviors[9,19,28]. This discomfort is often linked to high anxiety levels, commonly associated with symptoms like nausea and decreased appetite, leading individuals to adopt restrictive food intake as a maladaptive coping technique[11]. Regardless of their etiological value, GI symptoms often contribute to the continuation of the ED, so evaluating and addressing these issues should be a priority[23].

High levels of atopy were also found, such as food allergies and asthma, which raises suspicion for an immune-mediated disorder like eosinophilic esophagitis intensifying the symptomatology[22]. It is also important to note that young people with food allergies have high levels of anxiety associated with eating, which can be an underlying motive for the ED[28].

Regarding psychiatric comorbidities, the results converge across the different studies and also with the core literature in the field of psychiatry, which works to further enhance the reliability and validity of the findings[1]. Anxiety, neurodevelopmental disorders, mood disorders, and OCD were consistently the most prevalent comorbidities.

Children with anxiety may be more prone to developing particular phobias and avoidance behaviors, especially if they experience events such as choking or vomiting, which they might find more distressing due to their increased sensitivity to fear and anxiety-related responses[9]. This tendency is in line with the observed high prevalence of anxiety in various types of eating disorders[24]. In such cases, the tendency to avoid food can be attributed to underlying anxiety, or act as a coping mechanism to reduce such feelings, thereby negatively reinforcing these avoidance patterns[24]. Moreover, this overlap with anxiety disorders is evidenced by parental observations of ARFID patients, who often report separation anxiety. Supporting this link, research by Zanna et al. indicates that anxiety and worries during childhood can be predictors of eating disorders in adolescence[14]. The restrictive eating pattern can also increase the risk of suicide ideation and predict suicidality, although this has only been proven in females[20].

The elevated frequency of neurodevelopmental disorders can be explained by the cognitive rigidity and sensory sensitivity difficulties - hypersensitivity and exaggerated response to sensory stimuli present in ASD and ADHD[17,24]. ASD can influence and maintain ARFID, which suggests that this ED could be an indicator of ASD[17]. Zickgraf et al. also mention that the loss of appetite seen in some variations of this ED can be caused by the high rate of comorbidities. For example, stimulating medication for ADHD can cause appetite loss, as can depressive disorders[9].

ARFID patients also frequently experience nutritional deficiencies that lead to medical instability and consequently to a high rate of hospitalizations[10,11,13,17,19]. This should be tackled with early interventions and prompt diagnosis, which would ameliorate the effects of the food deprivation[12,17].

However, the highly heterogeneous presentation of the disorder, with its non-specific cadre of symptoms, can make this challenging[9,10,12,13,19,25,26,28]. To address these complexities, a multidisciplinary approach is paramount[17,23,27]. This should include a comprehensive assessment and care pathways encompassing medical nutrition, oral-motor skills, behavioral therapy, and sensory and environmental considerations[17]. Such a holistic intervention, tailored to each patient's needs, aims to improve resource planning, clinical management, and health outcomes[17]. Boerner et al. underscore the benefits of integrating physical and mental healthcare to address the mind-body connection in ARFID patients, highlighting the importance of multidisciplinary teams in managing the complex medical-psychosocial integration inherent in these disorders[23].

The impact of ARFID extends to the patients' families, causing psychological distress and interfering with parent-child relationships[10,19]. This stress is often heightened during mealtimes. Therefore, treatments should also include family involvement to support the patient's social and family interactions[27]. In view of ARFID's significant influence on the physical, sexual, and emotional development of patients, a holistic, family-inclusive approach is essential for a comprehensive treatment plan[17,23,28].

While this study presents compelling results, it is important to acknowledge its limitations. This systematic literature review predominantly includes studies conducted in North America and Europe, with a particular emphasis on specialized pediatric eating disorder clinics. This specificity in terms of geography and clinical setting, along with the exclusive emphasis on a pediatric population, raises concerns about the representativeness and applicability of the findings. Additionally, most of the studies included in the review are retrospective chart reviews, which may not capture the full spectrum of clinical experiences and can introduce bias due to their retrospective nature. This focus on specific regions, a particular age group, and limited settings suggests potential biases and limits the generalizability of the research to more diverse populations. Furthermore, the current literature reveals significant gaps, particularly in longitudinal perspectives and the exploration of various factors (biological, environmental, or otherwise) that contribute to ARFID. This narrow scope highlights the urgent need for more inclusive and diverse research methodologies to fully understand and address this complex disorder. From the risk of bias assessment, it is evident that while many studies exhibit a low risk of bias in certain domains, there is also a significant presence of moderate risk and areas lacking sufficient information to make a judgment. The prevalence of question marks across the matrix in figure 2 suggests that data for many domains was not adequately reported or was unclear, highlighting the need for more rigorous reporting standards in non-randomized studies. Conclusively, these visual tools collectively emphasize the varying levels of bias within the evaluated studies, underscoring the importance of thorough bias assessment in understanding the validity and reliability of study outcomes[29-31].

Future research on ARFID should strive for greater geographical diversity and varied methodological approaches to broaden our understanding and improve outcomes for those affected. Key areas for further investigation include conducting longitudinal studies to track ARFID's progression and long-term impacts, developing standardized assessment tools, and exploring its biological and environmental causes. Research should also focus on understanding ARFID's heterogeneity, examining its subtypes, and the high comorbidity with conditions like anxiety and GI and neurodevelopmental disorders. An integrated clinical approach involving various healthcare professionals is crucial, alongside personalized treatment strategies. Investigating the causal pathways between ARFID and its comorbidities, developing comprehensive screening tools, and conducting longitudinal studies on outcomes are also essential to enhance treatment and support for individuals with ARFID.

This systematic literature review, focusing on prevalent comorbidities in children and adolescents with ARFID, identified significant correlations between ARFID and GI, neurological, and immune disorders, as well as a range of psychiatric comorbidities like anxiety, neurodevelopmental disorders, OCD, and mood disorders. These findings align with existing literature and highlight a greater medical risk in this population compared to other eating disorders. The review emphasizes the need for early intervention and a multidisciplinary treatment approach due to ARFID's heterogeneous symptomatology. Given the complexity of ARFID, effective management extends beyond psychiatric care to involve pediatricians, gastroenterologists, endocrinologists, and other relevant medical specialists. This collaborative approach is crucial for comprehensive care, addressing the multifaceted nature of ARFID. Moreover, there is an urgent need to increase awareness and knowledge about ARFID among those who regularly interact with children and adolescents, such as educators and school health personnel. Training these individuals to recognize the early signs of ARFID can facilitate timely referrals and interventions, thus playing a pivotal role in improving outcomes for affected individuals. The impact of the disorder extends beyond the individual, affecting family dynamics and necessitating family-inclusive treatment plans.

Author contributions

F. Gomes Neves: Conception and design of the study, report, review or other type of work or paper; Acquisition of data either from patients, research studies, or literature; Analysis or interpretation of data either from patients, research studies, or literature; Drafting the article; Critical review of the article for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. D. Ferreira: Acquisition of data either from patients, research studies, or literature; Analysis or interpretation of data either from patients, research studies, or literature; Critical review of the article for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. P.C. Correia: Conception and design of the study, report, review or other type of work or paper; Analysis or interpretation of data either from patients, research studies, or literature; Drafting the article; Critical review of the article for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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