

**Common Comorbidities in
Avoidant/Restrictive Food Intake Disorder
among Children and Adolescents.
A systematic literature review**

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Medicina
(mestrado integrado)

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Declaração de Integridade

Eu, Francisca Gomes Fernandes Neves, que abaixo assino, estudante com o número de inscrição 41507 de Medicina da Faculdade de Ciências da Saúde, declaro ter desenvolvido o presente trabalho e elaborado o presente texto em total consonância com o **Código de Integridades da Universidade da Beira Interior**.

Mais concretamente afirmo não ter incorrido em qualquer das variedades de Fraude Académica, e que aqui declaro conhecer, que em particular atendi à exigida referenciação de frases, extratos, imagens e outras formas de trabalho intelectual, e assumindo assim na íntegra as responsabilidades da autoria.

Universidade da Beira Interior, Covilhã 12/02/2024

A handwritten signature in black ink, reading "Francisca Neves". The signature is written in a cursive style with a large initial 'F' and 'N'.

“É o momento muito raro em que, depois de termos enfrentado com sucesso uma prova, depois de um gesto corajoso, depois de um acto criador miraculoso, nos dizemos com satisfação, estupefactos: nunca teria pensado ser capaz.”

Elena Ferrante, em *A Invenção Ocasional*

Agradecimentos

Acabar este trabalho é estar a chegar ao fim de uma etapa da minha viagem. A todos os que ajudaram a moldar a Francisca que eu sou hoje, sem vocês o caminho não seria tão divertido.

À Dra. Paula Correia, pela sua disponibilidade constante, mesmo quando a vida lhe traz imprevistos. Pelo profissionalismo, sempre com sentido de humor e alegria. Trabalhar consigo é um prazer.

Ao Professor Dário pela sua rápida e valiosa contribuição.

À minha família por ser o melhor sítio onde crescer. Aos meus pais por estarem comigo em cada passo do caminho, sempre de braços abertos, prontos para me ajudar e confortar. À minha irmã, a minha parceira de sempre, por me ensinar que o mundo é pequeno e por toda a ajuda com a parte gráfica desta tese e de todos os outros trabalhos. Aos meus avós, que me incentivam sempre a ir mais longe. Às nossas gatas e à Canela, as mestres de comunicação não-verbal. Onde a vida me levar quero sempre voltar para a vossa beira.

Aos meus amigos, a todos, mas em especial às minhas Joanas. Juntos construímos uma nova casa.

Ao Jan, o meu companheiro, por tornares a vida tão colorida. Contigo tudo é possível!

Como diriam os Beach Boys, *God only knows what I'd be without you.*

Resumo

Introdução: A Perturbação de Ingestão Alimentar Evitante/Restritiva (ARFID-avoidant restrictive food intake disorder) é um diagnóstico novo de perturbação alimentar reconhecido pelo DSM-5 (2013) e pela CID-11 (2019). Esta revisão sistemática da literatura tem como objetivo reunir o conhecimento existente sobre as comorbidades mais comuns entre os doentes pediátricos com ARFID.

Métodos: Esta revisão sistemática da literatura, aderindo às diretrizes PRISMA, centrou-se nas comorbidades em participantes diagnosticados com ARFID, visando especificamente aqueles com uma idade média inferior ou igual a 18 anos. A pesquisa foi realizada, abrangendo o período de janeiro de 2013 a setembro de 2023, em duas bases de dados, PubMed e B-On, resultando na seleção de 20 estudos de um conjunto inicial de 161 artigos. O risco de *bias* foi analisado utilizando a ferramenta ROBINS-I.

Resultados: Relativamente às comorbidades médicas, 8 estudos continham informação relevante. Das comorbidades observadas, 38% eram sintomas gastrointestinais e 25% problemas neurológicos, incluindo enxaquecas e problemas sensoriais. Além disso, 10% das observações referem atingimento do sistema imunitário, como alergias alimentares e asma. As comorbidades psiquiátricas foram abordadas em 18 dos estudos incluídos. Entre as observações, as perturbações de ansiedade estavam presentes em 45%, as perturbações do neurodesenvolvimento, como a perturbação do espectro do autismo e a perturbação de hiperatividade e défice de atenção, em 33%, e as perturbações do humor em 15%. Os dados também identificaram outras condições médicas e psiquiátricas.

Conclusões: Esta revisão sublinha a associação entre ARFID e diversas comorbidades, incluindo doenças gastrointestinais, neurológicas e psiquiátricas, como as perturbações de ansiedade e de humor. Destaca-se 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. Demonstra-se ainda a necessidade de mais investigação para melhorar a compreensão e o tratamento de ARFID.

Palavras-chave

Perturbação de Ingestão Alimentar Evitante/Restritiva; Comorbilidades; Crianças; Adolescentes.

Abstract

Background and objectives: Avoidant/Restrictive Food Intake Disorder (ARFID) is a new feeding and eating disorder diagnosis recognized by the DSM-5 (2013) and ICD-11 (2019). This systematic literature review aims to gather existing knowledge on the most common comorbidities amongst pediatric ARFID patients.

Methods: This systematic literature review, adhering to PRISMA guidelines, focused on comorbidities in participants diagnosed with ARFID, specifically targeting those with a mean age below or equal to 18 years. A thorough search, covering the period from January 2013 to September 2023, was conducted across two databases, PubMed and B-On, resulting in the selection of 20 studies from an initial pool of 161 articles. The risk of bias was assessed using the ROBINS-I tool.

Results: In regards to medical comorbidities, 8 studies had relevant information. From the observed comorbidities, 38% involved gastrointestinal symptoms in ARFID patients, and 25% indicated neurological conditions including migraines and sensory issues. Additionally, 10% of observations noted immune system complications such as food allergies and asthma. Psychiatric comorbidities were addressed in all but two included studies. From the instances observed, anxiety disorders were present in 45%, neurodevelopmental disorders like autistic spectrum disorder and attention deficit hyperactivity disorder in 33%, and mood disorders in 15%. The data also identified several other medical and psychiatric conditions.

Conclusion: This review underscores the association between ARFID and diverse comorbidities, including gastrointestinal, neurological, and psychiatric conditions like anxiety and mood disorders. It highlights the disorder's complexity as well as its 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; Comorbidities; Child; Adolescents.

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List of Acronyms

ARFID	Avoidant/Restrictive Food Intake Disorder
DSM-5	The Diagnostic and Statistical Manual of Mental Disorders, Fifth edition
ICD-11	International Classification of Diseases, Eleventh revision
DSM-IV	The Diagnostic and Statistical Manual of Mental Disorders, Fourth edition
ED	Eating Disorders
AN	Anorexia nervosa
BN	Bulimia nervosa
PARDI	Pica, ARFID, and Rumination Disorder
PARDI-AR-Q	Pica, ARFID, and Rumination Disorder – ARFID Questionnaire
OCD	Obsessive compulsive disorder
ASD	Autistic spectrum disorder
ADHD	Attention deficit hyperactivity disorder
PRISMA	Preferred Reporting Items for Systematic-Reviews and Meta-Analysis
ROBINS-I	Risk of Bias In Non-randomized Studies of Interventions
USA	United States of America
UK	United Kingdom
PHP	Partial Hospitalization Program
CTED	Center for the Treatment of Eating Disorders
EDNOS	Eating Disorder Not Otherwise Specified
GI	Gastrointestinal
SSRD	Somatic Symptom and Related Disorder
FED	Feeding and eating disorder
BPM	Beats per minute
GAD	Generalized anxiety disorder

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MDD	Major depressive disorder
OSDD	Other specified dissociative disorder
PTSD	Post traumatic stress disorder

Introduction - What is ARFID?

Avoidant/Restrictive Food Intake Disorder (ARFID) is a new diagnosis recognized as a feeding and eating disorder in 2013, by the Fifth edition of The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (1). More recently, in 2019, it was also included in the 11th Revision of the World Health Organisation's International Classification of Diseases (ICD-11) (2).

This diagnosis describes a condition where individuals, regardless of age, have limited food preferences or avoid certain foods, replacing the previous diagnosis of "feeding disorder of infancy or early childhood" from the DSM-IV, which was only applicable to children aged 6 years or younger (1).

Diagnostic criteria and features

ARFID is a feeding and eating disorder diagnosed by avoidance or restriction of food intake that lead to significant weight loss, nutritional deficiencies, dependence on enteral feeding or oral nutritional supplements, or marked interference with psychosocial functioning (criteria A) (1).

The diagnostic criteria are made explicit below in Table 1. DSM-5 criteria are in agreement with ICD-11 criteria.

According to the DSM-5, there are three different phenotypes/motivational factors for food avoidance: lack of interest in food or eating, fear of aversive consequences (such as choking), increased sensitivity to sensory aspects of food (such as texture, color, smell, temperature, appearance or taste) (1). These profiles are not incompatible with each other, meaning that an individual can fall into more than one (3–5). This was described by Thomas et. al as a tridimensional model where each individual with ARFID would be placed in a different point on a 3-dimensional scale, illustrating how profiles can coexist and vary in severity and degree (3).

In contrast to the most commonly studied eating disorders (EDs), anorexia nervosa (AN) and bulimia nervosa (BN), there is no drive to lose weight and no concern with body image and size. Also, it cannot be explained by food insecurity (lack of availability of food) or customs and traditions related to a specific culture. Lastly, it cannot be linked to

a coexisting medical condition or clarified by any other mental disorder. If it does occur alongside another condition or disorder, it is more severe than what is typically associated with that condition or disorder (1).

Table 1- DSM-5 & ICD-11 diagnostic criteria for ARFID.

Diagnostic Criteria	
A	An eating or feeding disturbance (e.g., apparent lack of interest in eating or food; avoidance based on the sensory characteristics of food; concern about aversive consequences of eating) characterized by avoidance or restriction of food associated with one (or more) of the following: <ol style="list-style-type: none"> 1. Significant weight loss (or faltering growth in children or failure to achieve expected weight gain). 2. Clinically significant nutritional deficiency. 3. Reliance on tube feeding or oral nutritional supplements. 4. Significant impairment in social, personal, family, educational, occupational and psychological functioning.
B	The eating pattern cannot be explained by unavailability of food or by practices associated with a cultural context.
C	The eating pattern is distinct and does not manifest solely during episodes of anorexia nervosa or bulimia nervosa. There is no accompanying concern with body weight or body shape.
D	The eating pattern is not a result of any coexisting medical conditions or more accurately described by another mental health disorder. If the pattern appears alongside another condition or disorder, it is of a severity that goes beyond what is commonly seen with that condition or disorder, thus requiring further clinical attention.

Adapted from: American Psychiatric Association, Diagnostic and statistical manual of mental disorders: DSM-5. 5th ed. Washington, D.C: American Psychiatric Association; 2013 & International Classification of Diseases, Eleventh Revision (ICD-11), World Health Organization (WHO) 2019/2021 <https://icd.who.int/browse11> (1,2)

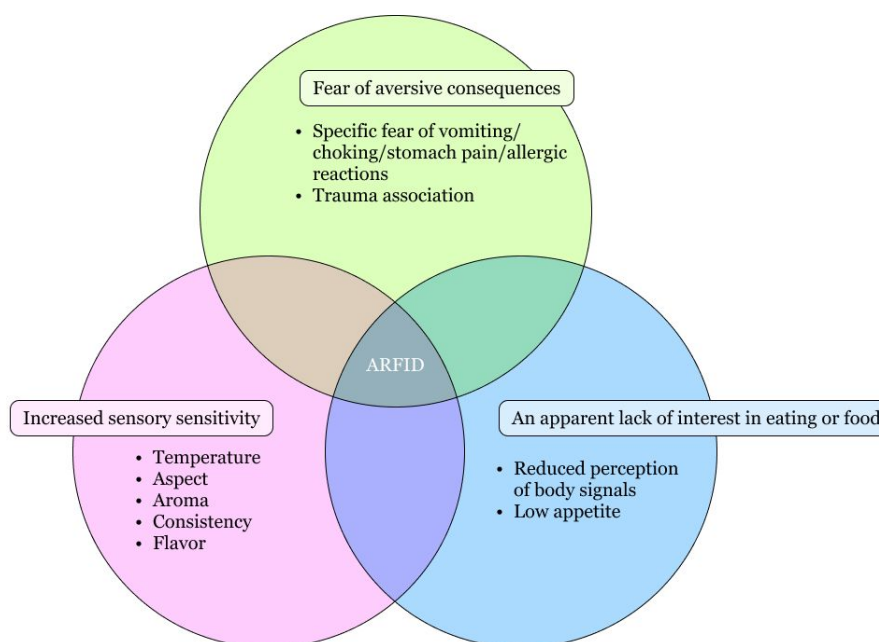


Figure 1-The three ARFID presentations.

Adapted from: Thomas JJ, Lawson EA, Micali N, Misra M, Deckersbach T, Eddy KT. Avoidant/Restrictive Food Intake Disorder: a Three-Dimensional Model of Neurobiology with Implications for Etiology and Treatment. *Curr Psychiatry Rep.* 2017 Aug;19(8):54. (5)

Epidemiology

Literature on the epidemiology of ARFID in the pediatric age is very limited. However, there is a systematic review from Sanchez-Cerejo et. al, that summarizes the available studies until 2022 (6).

Most of the data comes from a specialized pediatric eating disorder treatment setting, where the prevalence ranges from 5% to 22,5%. In a general pediatric service, it was observed in 3% of the cases in an outpatient sample and 7,2% in an inpatient sample. Two studies from a pediatric gastroenterology clinic reported a prevalence of 1,5% to 8% while one from a pediatric gynecology clinic reported 3,7%. The highest prevalence is found in specialized tertiary care services for feeding problems with a range from 32% to 64%. A part of the included studies was from non-clinical samples with a range of 0,3% to 15,5% (6).

A Canadian study, based on the Canadian Pediatric Surveillance Program, collected data referring to ARFID in children and adolescents aged 5-18. They reported an overall incidence of 2,02% in that age group, specifically 2,5% in females and 1,5% in males (7).

More recently, a Dutch population-based study using the Generation-R sample (a population-based cohort from early pregnancy onward in Rotterdam, the Netherlands), also gathered significant data regarding ARFID. Out of 2,862 children, 6,4% (n=183) had ARFID symptoms (8).

Several studies have shown that ARFID patients tend to be younger when initially observed: mean age ranging from 11,1 to 14,6, in comparison to 14-15,6 in AN and 14,9-16,7 in BN (8-10). In addition, this diagnosis is typically more frequent in males when confronted with other eating disorders (9–13).

An opinion universally held in all studies is that the lack of consistent data on prevalence and incidence stems from a great heterogeneity of screening methods. Even though there are some tools available, such as PARDI (Pica, ARFID, and Rumination Disorder Interview), PARDI-AR-Q (Pica, ARFID, and Rumination Disorder – ARFID Questionnaire) (14-15), it is still missing one that is standardized (6,8).

Assessment

When ARFID was introduced as a diagnosis in DSM-5, there were no assessment methods available. In the last 10 years, some diagnostic tools were developed and introduced. However, it is still lacking one that is uniform.

In Table 2., four structured interviews and four self-report methods are summarized.

Table 2- Assessments for ARFID.

	Short	Assesses for the different ARFID presentations	Measures ARFID severity	Approved for use in ARFID	Facilitates the differential diagnosis with other EDs	Evaluates changes before and after ARFID treatment
Structured clinical interviews						
EDA-5 (Sysko et al., 2015)	x				x	
SCID-5 (First et al., 2014)					x	
EDE – ARFID Module (Schmidt et al., 2019)	x	x		x	x	
PARDI (Bryant-Waugh et al., 2019)		x	x	x		x
Self-report questionnaires						
FNS (Pliner & Hobden, 1992)	x					x
NIAS (Zickgraf & Ellis, 2018)	x	x		x		x
PARDI-AR-Q (Bryant-Waugh et al., under revision)	x	x	x	x		x
EDY-Q (Kurtz et al., 2015)	x	x		x	x	

EDA-5, Eating Disorder Assessment for DSM-5; SCID-5, Structured Clinical Interview for DSM-5; EDE, Eating Disorder Examination; PARDI, Pica, ARFID, and Rumination Disorder Interview; EDE-Q, Eating Disorder Examination – Questionnaire; FNS, Food Neophobia Scale; NIAS, Nine-Item ARFID Screen; PARDI-AR-Q, Pica, ARFID, and Rumination Disorder – ARFID Questionnaire

Adapted from: Kambanis PE, Thomas JJ. Assessment and Treatment of Avoidant/Restrictive Food Intake Disorder. *Curr Psychiatry Rep.* 2023 Feb;25(2):53-64. (16)

Intervention and treatment

While there is no universally acknowledged and standardized treatment approach for ARFID, extensive research has been conducted in this field. A view that is often shared among them is the general necessity for a multidisciplinary team, as ARFID is a very heterogeneous disorder (5,16-17).

Data from recent years was summarized by Archibald et. al, which concluded that the core intervention strategy should be a psychological approach. This can be either family-based or cognitive behavioral therapy - both proved to be efficient and neither was better than the other.

Dietetic interventions, which require an adjustment depending on the reason behind food avoidance, have also been studied. For example, if an individual has a sensory or aversive food avoidance, preferred foods should be offered first, gradually followed by the less preferred ones.

Medical and pharmacological approaches may also be required. The use of D-cycloserine - to reduce aversion, olanzapine - to increase cognitive flexibility, and mirtazapine, fluoxetine, buspirone, and lorazepam - to mitigate anxiety related to eating, have shown to be effective in the management of ARFID (5).

Comorbidities

In the DSM-5 it is reported that the most common comorbidities are anxiety disorders, obsessive-compulsive disorder, and neurodevelopmental disorders (specifically autism spectrum disorder, attention-deficit/hyperactivity disorder, and intellectual developmental disorder [intellectual disability]) (1).

In this review, recent studies are going to be analyzed to reinforce the existing knowledge on the subject.

Objectives

Since the diagnosis was introduced in the most recent version of the DSM - the DSM-5 - there has been growing clinical and scientific interest in the disorder. The burgeoning literature is still insufficient for the integration of fully evidence-based practice (3). As such, it is timely to do systematic reviews to gather available data.

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 (18).

A first search was conducted in July 2023 and the final search was on the 5th of September of 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, which was published in 2013. Consequently, 2013 was the starting point for the search.

Using the keywords "Avoidant/Restrictive Food Intake Disorder", "Comorbidities", "Child", "Adolescent", 70 articles were identified in Pubmed and 91 in B-On. After the removal of 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 (4,9,10,13,19–33).

This analysis was further enriched by consulting reference books in the field of child psychiatry.

The review selection process is summarized in the PRISMA Flow diagram in Figure 2.

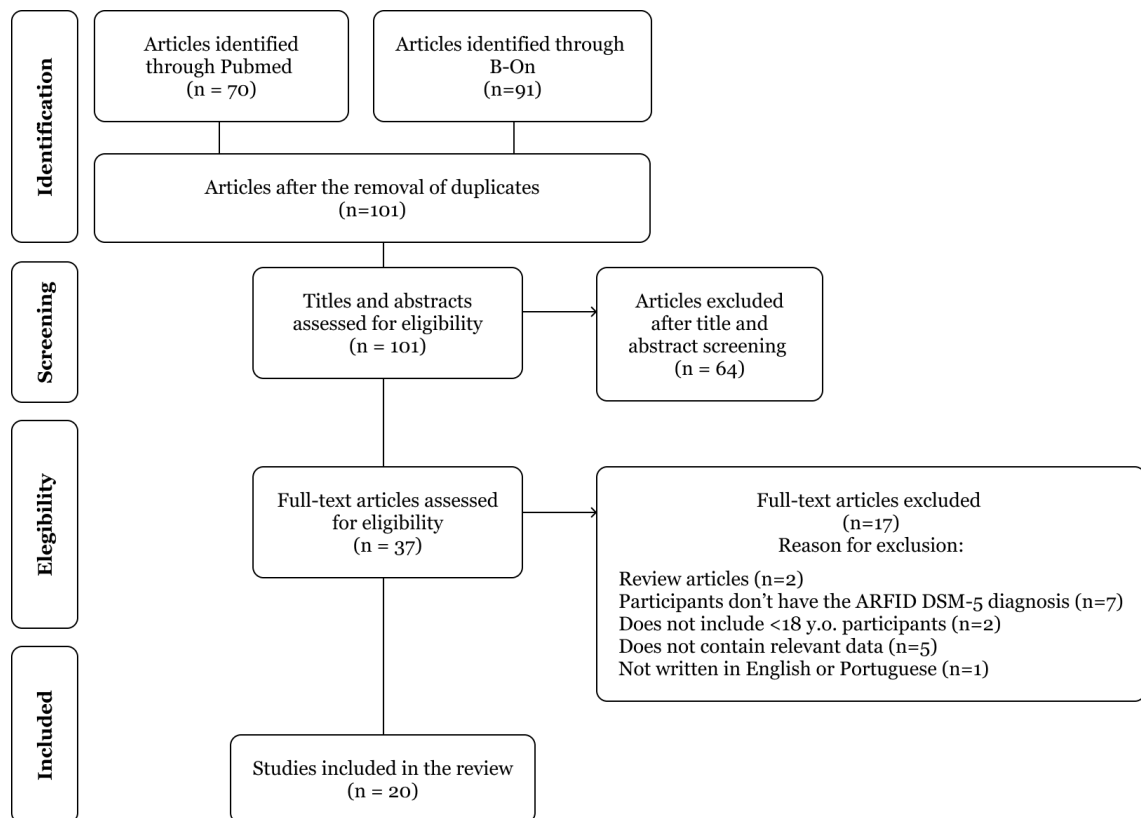


Figure 2-Flow diagram of reviewed studies, according to PRISMA. (18)

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 DSM5 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 mean age of participants above 18 years old.

Data extraction

Data from each article was extracted referring to 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.

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 and an overall risk of bias (34,35).

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, diagnosed with ARFID, using DSM-5 or ICD-11 criteria.

Key aspects of the included studies are presented in Table 3 and Table 4.

Characteristics of the Included Studies

The majority were conducted in North America (n=10) - USA (n =5) (4,13,20,23,31) and Canada (n=5) (10,12,28,32,33) - and four carried out in multiple countries (9,25,27,29). Two studies took place in Japan (21,30) and four in Europe: United Kingdom (22), Italy (19), Spain (24) and Germany (26).

All of the included studies focused on clinical populations with most drawing on samples from pediatric eating disorders specialized services (n=11) (4,9,10,12,13,19,20,22,24,28,32) and utilizing retrospective chart reviews (n=11) (4,9,10,12,13,19,21,23,28,31,32). 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 3, which utilizes a traffic light color-code to evaluate individual studies across seven domains of bias and an overall appreciation. Figure 4 summarizes this data into a bar chart, quantitatively presenting the overall proportion of studies falling into low, moderate, or unknown risk categories for each bias domain. From these assessments, 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 determination. The prevalence of question marks across the matrix 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.

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Table 3- Characteristics of the included studies

Author, year & 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 (4)	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 (19)	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 to September 2017, and later reclassified to DSM-5 criteria by an expert.	Participants were children and adolescents under 18 years old, initially diagnosed based on DSM-IV with Anorexia Nervosa, Feeding Disorder of Infancy or Early Childhood, or Eating Disorder Not Otherwise Specified Diagnosis later reclassified to 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 (20)	Longitudinal study	Data collection was done through interviews, pen-and-paper assessments, and electronic health records.	Patients aged 7-19 years 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 to 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 (21)	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.

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Author, year & country	Design	Method	Sample description	Sample setting	Sample size	Sample Gender	Sample Age	How was the ARFID diagnosis made?
Fadila Farag et al. (2022) UK (22)	Cross-sectional	Data collected prospectively from patients seen by the tertiary feeding service.	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 (23)	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.
Laura Cañas et al. (2020) Spain (24)	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 hospitalization n=4)	♂ n=20 ♀ n=13	7-17 (mean of 10,8 y.o.)	DSM-5 criteria.
Martin M. Fisher et al. (2013) USA & Canada (9)	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.

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Author, year & country	Design	Method	Sample description	Sample setting	Sample size	Sample Gender	Sample Age	How was the ARFID diagnosis made?
Melissa Lieberman et al. (2018) Canada (33)	Observational study.	Data was collected through clinical interviews, psychometric questionnaires, and chart reviews.	In- and outpatient who met the DSM-5 criteria for Anorexia Nervosa (AN) and Avoidant/Restrictive Food Intake Disorder (ARFID), between May 2013 and January 2017, that were part of the specialized program COPE at the Hospital for Sick Children in Toronto.	Specialized program for children under 13.	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 in 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 (25)	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 (26)	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.

Common Comorbidities in Avoidant/Restrictive Food Intake Disorder among Children and Adolescents.

Author, year & 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 (10)	Cross-sectional	Retrospective chart review of patients diagnosed with food avoidant emotional disorder, childhood anorexia nervosa, 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.	Paediatric ED treatment programme.	n=34	♂ n=7 ♀ n=27	(mean of 13,7 y.o.)	DSM-5 criteria.
Anna Aulinas et al. (2021) USA, Spain & Switzerland (27)	Cross-sectional	Data was collected from studies investigating the neurobiology of restrictive eating disorders.	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 (28)	Retrospective chart review.	Data was collected through a retrospective review of medical records.	Patients diagnosed with ARFID or a gastrointestinal (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 programme for children and adolescents with EDs between August 2008 and May 2012.	Day programme for EDs.	n=39	♂ n=8 ♀ n=31	7-17 (mean of 11,1 y.o.)	DSM-5 criteria.

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Author, year & country	Design	Method	Sample description	Sample setting	Sample size	Sample Gender	Sample Age	How was the ARFID diagnosis made?
Evelyna Kambanis et al. (2019) USA & Switzerland (29)	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 (30)	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 (31)	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 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 (32)	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.

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Table 4- Results from the included studies.

Author, year & country	Medical comorbidities	Psychiatric comorbidities	Other findings
Hana F. Zickgraf et al. (2019) USA (4)	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 DSM-5 A1(weight loss) n=67 A1 (growth failure) n=11 A2 (restricted nutrition) n=78 A3(supplement dependent) n=28
Valeria Zanna et al. (2020) Italy (19)	No reference	Anxiety disorder n=33 Mood disorder n=15	
Helene Keery et al. (2019) USA (20)	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 (21)	No reference	Developmental Disorders n=6	Family history of mental disorders n=6

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Author, year & country	Medical comorbidities	Psychiatric comorbidities	Other findings
Fadila Farag et al. (2022) UK (22)	No reference	ASD n=144	
Sarah E. Strandjord et al. (2015) Canada (23)	No reference	Unspecified psychiatric comorbidity n=5	Family history: Eating disorder n=3 Other psychiatric disorder n=9
Laura Cañas et al. (2020) Spain (24)	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 DSM-5: A1 (significant weight loss or growth failure) 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 (9)	Unspecified medical condition related to the disease n=34 unrelated to the disease n=16 *Refers 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 Obsessive Compulsive Disorder n=6	
Melissa Lieberman et al. (2018) Canada (33)	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%)

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Author, year & country	Medical comorbidities	Psychiatric comorbidities	Other findings
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 DSM-5: A1 (significant weight loss or growth failure) 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 (25)	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%) Posttraumatic 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%)	

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Author, year & country	Medical comorbidities	Psychiatric comorbidities	Other findings
Dominik Düplois et al. (2023) Germany (26)	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 (10)	No reference	GAD n=17 MDD n=4 *Other diagnoses including panic disorder, obsessive compulsive disorder, and social phobia were present but no mention of values.	Immediate family member with a diagnosed psychiatric disorder n=5
Anna Aulinas et al. (2021) USA, Spain & Switzerland (27)	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 (28)	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%)	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%)	This study compared characteristics of pediatric patients diagnosed with ARFID to those with gastrointestinal (GI)-related SSRD. 16% of the total sample reported symptoms consistent with co-occurring diagnoses of ARFID and SSRD

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Author, year & country	Medical comorbidities	Psychiatric comorbidities	Other findings
	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%)	<p>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%)</p> <p>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%)</p>	
Terri A Nicely et al. (2014) USA (13)	<p>Symptoms & 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%)</p>	<p>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%)</p>	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.
Evelynna Kambanis et al. (2019) USA & Switzerland (29)	No reference	<p>Anxiety, Obsessive-Compulsive, 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%) OCD- C n=3 (4,0%) / L n=3 (4,0%) Agoraphobia- current n=1 (1,0%) / lifetime 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%)</p>	<p>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, and conduct disorder;</p> <p>The fear of aversive consequences profile was associated with more than twice the odds of a current comorbid anxiety, obsessive compulsive, and trauma-related disorder;</p> <p>The ARFID sensory sensitivity profile was associated with nearly three times the odds of a current or lifetime</p>

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Author, year & country	Medical comorbidities	Psychiatric comorbidities	Other findings
		<p>PTSD- C n=0 (0,0%) / L n= (1,0%)</p> <p>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%)</p> <p>Suicidality: Total- C n= 6 (8,0%) / L n= 10 (14,0%)</p> <p>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%)</p> <p>Eating Disorders and Substance-Related Disorders: Total- C n= 0 (0,0%) / L n= 1 (1,0%) Binge eating disorder: current n=0 (0,0%) / lifetime n= 1 (1,0%)</p> <p>Schizophrenia Spectrum and Other Psychotic Disorders: Total- C n=0 (0,0%) / L n=0 (0,0%)</p>	<p>comorbid anxiety, obsessive-compulsive, and trauma-related disorder;</p> <p>The sensory sensitivity profile was associated with more than twice the odds of a lifetime comorbid depressive and bipolar-related disorder;</p> <p>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, obsessive-compulsive, and trauma-related disorders.</p>
Takeshi Inoue et al. (2021) Japan (30)	No reference	ASD n=4 (12,5%)	

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Author, year & country	Medical comorbidities	Psychiatric comorbidities	Other findings
Kamryn T. Eddy et al. (2015) USA (31)	<p>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</p>	No reference	
Mark L. Norris et al. (2021) Canada (32)	No reference	<p>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%)</p> <p>ASD: ARFID total n=16 (23,1%) Aversive n=1 (16,7%) Sensory n=1 (50,0%) Low appetite, limited interest n=0 (0,0%) ARFID-Mixed n=4 (40,0%)</p> <p>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%)</p> <p>Learning difficulties: ARFID total n=8 (30,08%) Aversive n= 1 (16,7%) Sensory n=0 (0,0%)</p>	<p>Patients with aversive presentations presented an abbreviated course of illnesses and were all diagnosed with anxiety.</p> <p>Patients with low appetite represented the highest proportion of single-symptom presentations.</p> <p>Patients 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</p>

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Author, year & country	Medical comorbidities	Psychiatric comorbidities	Other findings
		<p>Low appetite, limited interest n=3 (37,5%) ARFID-Mixed n=4 (40,0%)</p> <p>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%)</p> <p>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%)</p>	

Study	Risk of bias domains							Overall
	D1	D2	D3	D4	D5	D6	D7	
Hana F. Zickgraf et al. (2019) USA	+	+	?	?	?	+	+	+
Valeria Zanna et al. (2020) Italy	+	+	?	?	?	+	+	+
Helene Keery et al. (2019) USA	-	+	?	?	?	-	+	-
Isaku Kurotori et al. (2019) Japan	+	+	?	?	?	+	+	+
Padma Parag et al. (2022) UK	+	+	?	?	?	+	+	+
Sarah E. Strandjord et al. (2015) Canada	+	-	?	?	?	+	+	+
Laura Cañas et al. (2020) Spain	+	-	?	?	?	+	+	-
Martin M. Fisher et al. (2013) USA & Canada	+	+	?	?	?	+	+	+
Melissa Lieberman et al. (2018) Canada	+	+	?	?	?	-	+	-
Megan Cooney et al. (2018) Canada	+	+	?	?	?	+	+	+
Evelyna Kambanis et al. (2022) USA, Switzerland & UK	+	?	?	?	?	+	+	+
Dominik Düplois et al. (2023) Germany	-	+	?	?	?	-	+	-
Mark L. Norris et al. (2014) Canada	+	+	?	?	?	+	+	+
Anna Aulinas et al. (2020) USA, Spain & Switzerland	-	-	?	?	?	-	-	-
Katelynn E Boerner et al. (2021) Canada	-	+	?	?	?	-	-	-
Terri A Nicely et al. (2014) USA	+	+	?	?	?	+	+	+
Evelyna Kambanis et al. (2020) USA & Switzerland	+	+	?	?	?	+	+	+
Takeshi Inoue et al. (2021) Japan	+	+	?	?	?	-	+	-
Kamryn T. Eddy et al. (2015) USA	+	-	?	?	?	+	+	-
Mark L. Norris et al. (2021) Canada	+	+	?	?	?	+	+	+

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
- Moderate
+ Low
? No information

Figure 3- Traffic-light plot with the domains of the risk of bias assessment for each study, using the ROBINS-I tool (34,36).

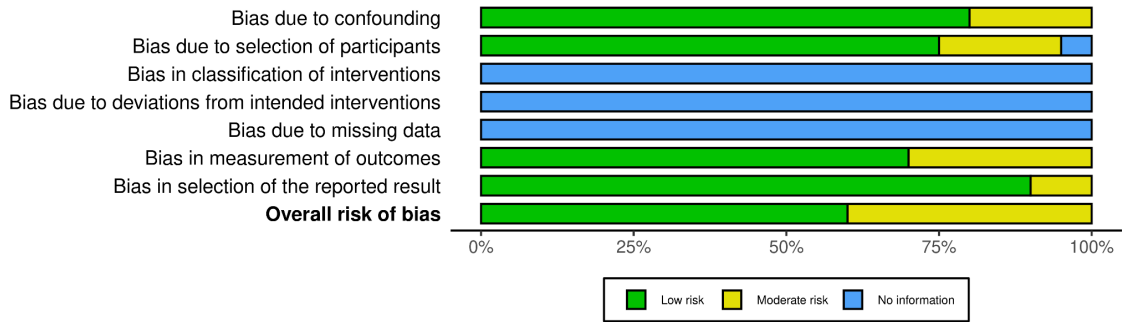


Figure 4- Bar diagram with quantitative summary of the domains of the risk of bias assessment, using the ROBINS-I tool (34,36).

Results from the included studies - Medical Comorbidities

From the 20 selected studies, 8 provided data on medical comorbidities, giving a total sample of 383 ARFID patients who were assessed for these comorbid conditions (4,9,13,26–28,31,33). However, only 353 observations of comorbidities were recorded. Due to consistent methodology employed across the studies, the results were aggregated to provide a more robust body of evidence.

All eight studies address Gastrointestinal symptoms or conditions, revealing that about 38% of observations indicate a related complaint or disease. Among these observations, 117 instances reported GI symptomatology, 56 referred either to diarrhea or gastroesophageal reflux or early satiety or nausea or gastroparesis or abdominal pain and 61 did not specify. Another fourteen observations involved a GI disease diagnosis, 7 with either chronic abdominal pain or inflammatory conditions and 7 not specifying.

Secondly, 25% of the observations indicate a neurological associated condition. Among the patients, sensory problems were reported twenty-three times. Eighteen instances mentioned experiencing migraines, cognitive impairment was reported seventeen 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, respectively, nineteen and six instances. Asthma was documented in nine observations and atopic dermatitis in one.

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

Results from the included studies - Psychiatric Comorbidities

All but two studies reported on psychiatric comorbidities, giving a total sample of 1125 participants analyzed for psychiatric comorbidities (4,9,10,12,13,19–26,28–33). However, only 924 observations of comorbidities were recorded. Due to consistent methodology employed across the studies, the results were aggregated to provide a more robust body of evidence.

From this instance pool, 45% of the observations recorded anxiety disorders, more specifically, 88 instances for generalized anxiety disorder (GAD), 19 a specific phobia, 14 social anxiety disorder with the same number reporting panic disorder, 4 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 a diagnosis in 179 instances, attention deficit hyperactivity disorder (ADHD) in 68, a learning disability in 15 and 40 reported on 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 referred a co-occurring diagnosis of obsessive-compulsive disorder (OCD), 11 instances a suicidal behaviour, 5 a conduct disorder, 1 a dissociative disorder and 10 an unspecified psychiatric disorder.

Additionally, three studies reported on psychiatric history (20,27,29), four on family's psychiatric and eating disorder history (10,21,23,27), two on the use of psychiatric medication (20,27), one showed data on history of abuse, self-harm and substance use

(28) and one evaluated the distribution of psychiatric comorbidities in the different ARFID phenotypes (32).

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 on the criteria A from the DSM-5 diagnostic criteria, showing the frequency of each one in their sample (4,12,24). Due to 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 those 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 A4 criteria (marked interference with psychosocial functioning).

Keery et. al reported signs of medical instability such as, bradycardia, hypotension, orthostatic instability, and amenorrhea (20).

While Lieberman et. al found that some participants had an infection prior to the onset of the eating disorder, Cooney et. al investigated in each participant what was the trigger for the eating disorder (12,33).

Another interesting finding, according to Nicely et. al, was that although individuals with ARFID do not have body distortion (as seen in AN), 21% of the participants from that study had 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 (29,32). Participants with lack of interest in food phenotype are more likely to have one single symptom at presentation. Participants with aversive phenotype have a more abbreviated course of illness and are twice as likely as the other phenotypes to have comorbid anxiety, obsessive compulsive, and trauma-related disorder. Participants with sensory sensitivity phenotype are three times as likely as the other phenotypes to have comorbid anxiety, obsessive-compulsive, 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 is a significant number of comorbidities amongst young individuals with ARFID (9,24,26,33). This is congruent with other literature that finds a greater medical risk in this population, in comparison with other EDs (24).

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 (28). GI problems can cause discomfort during eating, potentially influencing food avoidance or restrictive behaviors (4,24,33). 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 (10). 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 (28).

High levels of atopy were also found, like food allergies and asthma, which raises suspicion for an immune mediated disorder like eosinophilic esophagitis intensifying the symptomatology (27). 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 (33).

Regarding the psychiatric comorbidities, the results converge across the different studies and also with the core literature in the field of psychiatry, which work to further enhance the reliability and validity of the findings (1). Anxiety, neurodevelopmental disorders, OCD and mood disorders 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 (4). This tendency is in line with the observed high prevalence of anxiety in various types of eating disorders (29). 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 (29). Moreover, this overlap with anxiety disorders is evidenced by parental observations of ARFID patients, which 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 (19). The restrictive eating pattern can also increase the risk of suicide ideation and predicts suicidality, although only proven in females (25).

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 (22,29). ASD can be an influencing and maintaining factor for ARFID, which suggests that this ED could be an indicator of ASD (22). Zickgraf et. al also mention that appetite loss 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 (4).

ARFID patients also frequently experience nutritional deficiencies that lead to medical instability and consequently to a high rate of hospitalizations (9,10,13,22,24). This should be tackled with early interventions and prompt diagnosis, that would ameliorate the effects of the food deprivation (12,22).

However, the highly heterogeneous presentation of the disease, with its non-specific cadre of symptoms, can make this challenging (4,9,12,13,24,30,31,33). To address these complexities, a multidisciplinary approach is paramount (22,28,32). This should include a comprehensive assessment and care pathways encompassing medical nutrition, oral-motor skills, behavioral therapy, and sensory and environmental considerations (22). Such a holistic intervention, tailored to each patient's needs, aims to improve resource planning, clinical management, and health outcomes (22). Boerner et. all 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 (28).

The impact of ARFID extends to the patients' families, causing psychological distress and interfering with parent-child relationships, (9,24). This stress is often heightened during

mealtimes. Therefore, treatments should also include family involvement to support the patient's social and family functioning (32). Recognizing 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 (22,28,33).

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 highlight on specialized pediatric eating disorder clinics. This geographical and clinical setting specificity, along with the exclusive emphasis on a pediatric population, raises concerns about the representativeness and applicability of the findings. Additionally, the majority of studies included in the review are retrospective chart reviews, which may not capture the full spectrum of clinical experiences and can introduce biases due to their retrospective nature. This focus on specific regions, age group and setting 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.

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, gastrointestinal 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.

Conclusion

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. Additionally, 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 early signs of ARFID can facilitate timely referrals and interventions, thus playing a pivotal role in improving outcomes for affected individuals. The disorder's impact extends beyond the individual, affecting family dynamics and necessitating family-inclusive treatment plans.

Future studies should aim to broaden the understanding of ARFID, exploring its biological and environmental causes, and developing more comprehensive assessment and treatment strategies to improve outcomes for those affected by this complex condition.

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