BMJ Paediatrics Open

Physical health complications in children and young people with avoidant restrictive food intake disorder (ARFID): a systematic review and meta-analysis

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To cite: James RM, O'Shea J, Micali N, *et al*. Physical health complications in children and young people with avoidant restrictive food intake disorder (ARFID): a systematic review and meta-analysis. *BMJ Paediatrics Open* 2024;**8**:e002595. doi:10.1136/bmjpo-2024-002595

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjpo-2024-002595).

Received 28 February 2024
Accepted 18 June 2024

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ABSTRACT

Background Avoidant restrictive food intake disorder (ARFID) is a feeding and eating disorder with known acute and longstanding physical health complications in children and young people (CYP) and commonly presents to paediatricians.

Objective To systematically review the published literature on physical health complications in CYP with ARFID using Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Methods A systematic search of PubMed, Embase, Web of Science, PsycINFO and Cochrane Library was performed on 14 February 2024. Studies reporting physical health complications in CYP ≤25 years with ARFID were included. We pooled studies for meta-analysis comparing ARFID with healthy controls or anorexia nervosa (AN).

Results Of 9058 studies found in searches, we included 132 studies. We found evidence for low weight, nutritional deficiencies and low bone mineral density. CYP with ARFID can present across the weight spectrum; however, the majority of CYP with ARFID were within the healthy weight to underweight range. Most studies reported normal range heart rates and blood pressures in ARFID, but some CYP with ARFID do experience bradycardia and hypotension. CYP with ARFID had higher heart rates than AN (weighted mean difference: 12.93 bpm; 95% CI: 8.65 to 17.21; n=685); heterogeneity was high (I^2: 81.33%).

Conclusion There is a broad range of physical health complications associated with ARFID requiring clinical consideration. Many CYP with ARFID are not underweight yet still have complications. Less cardiovascular complications found in ARFID compared with AN may be related to chronicity.

PROSPERO registration number CRD42022376866.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Avoidant restrictive food intake disorder (ARFID) is a feeding and eating disorder which often results in malnutrition and its consequent physical health complications in children and young people (CYP).

WHAT THIS STUDY ADDS

⇒ CYP with ARFID can present across the whole weight spectrum; ARFID is not exclusively a low-weight eating disorder.
⇒ CYP with ARFID are at risk of several other complications such as low bone mineral density and nutritional deficiencies which do not discriminate based on the individuals weight.
⇒ CYP with ARFID on average present with higher heart rates and lower levels of hypotension and bradycardia than individuals with anorexia nervosa (AN), despite similar levels of underweight.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our review has highlighted the need for comprehensive physical health checks for every individual with ARFID, regardless of their weight status.
⇒ Our review has also highlighted the need for a more nuanced approach when assessing for risk in CYP with ARFID compared with what is currently in use for AN.
⇒ There are some critical gaps in the literature that warrant further study such as longitudinal analysis and more representative samples.

INTRODUCTION

Avoidant restrictive food intake disorder (ARFID) is a feeding and eating disorder (ED) characterised by persistent restricted intake in quantity or variety of food.[1] Such restrictive feeding results in one or more of: a failure to meet nutritional or energy needs; dependence on oral or enteral supplements and/or significant impacts on psychosocial functioning.[1] Three non-mutually exclusive presentations tend to motivate food-related behaviour in ARFID: (1) lack of interest in food or lack of appetite; (2) sensory sensitivity to food (eg, based on foods texture, appearance and smell) and (3) fear of the consequences of food (eg, choking, vomiting).[1]

Consequently, ARFID is distinct from anorexia nervosa (AN) as the driving motivations behind the eating behaviour noticeably lack a focus on body weight or image.[1] The onset of ARFID is usually in childhood (<12 years of age),[2] with a prevalence between 3.2% and 15.5% in primary school-aged children and ~0.5% across all ages.[2]

While ARFID is considered primarily a psychological disorder, persistent feeding behaviour regularly results in failure to meet energy/nutritional needs[1] leading to physical complications carrying a range of potential risks. These can be acute when weight loss leads to cardiovascular and temperature instability,[3] or more longstanding, leading to growth faltering and low bone mineral density (BMD).[4] Such physical impacts mean that children and young people (CYP) with ARFID commonly present to paediatricians, and knowledge of physical health assessment and management is essential for those working medically with CYP.

As ARFID is a relatively new diagnosis (first defined in 2013[1]), research has emerged later than for other EDs, and so more established physical health findings from AN (given restricted intake) have been applied as a model, in particular to acute risk assessment.[5] This is potentially problematic due to important differences between ARFID and AN, meaning that such application may not be valid. ARFID tends to have an earlier age of onset, malnutrition is generally more longstanding and there are specific food avoidances leading to nutritional deficiencies.[2] A larger body of published evidence on the physical impact of ARFID in CYP has emerged, providing opportunity for a synthesis of the literature to aid better prediction, prevention, tailor clinical treatments and identify important areas for further research. A systematic review on this topic has not been published before. We conducted a systematic review of the published literature and meta-analyses using Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines[6] to examine for both acute and chronic physical health risks in CYP with ARFID.

METHODS

Search strategy

We searched for published full-text articles on ARFID with any physical health complication in PubMed, Embase, Web-of-Science, PsycINFO and The Cochrane Library from database inception to 14 February 2024. Relevant search terms for ARFID and physical health were used for each electronic database (online supplemental file 1). We also conducted citation searches of included studies. We registered a broader systematic review for physical health complications in ARFID in all ages with PROSPERO, and here we present only the findings for CYP (≤25 years of age).

Inclusion criteria were: (1) peer-reviewed full-text publications reporting any kind of primary data on physical health parameters in individuals with ARFID except for non-systematic reviews; (2) studies containing one or more participants ≤25 who had been diagnosed with ARFID before or at the time of publication; (3) studies in any language; (4) studies from any geographical area.

Exclusion criteria were: (1) studies mixing adults with CYP throughout reporting; (2) studies not including any data on physical complications in ARFID; (3) studies only reporting physical complications caused by comorbidities of ARFID or other pre-existing conditions.

Two researchers (RMJ and JO) independently screened titles and abstracts for inclusion using the online systematic review tool, Covidence. Once an agreement was met, full-text articles were screened independently for inclusion. LDH provided adjudication on disagreement.

Data extraction and quality assessment

We extracted data using a customised form: (1) general study information; (2) general characteristics of participants; (3) anthropometric measurements (weight, standardised weight for age (weight z-score), body mass index (BMI), standardised BMI for age (BMI z-score) or percentage median BMI (%MBMI, % of subject BMI of median BMI for age and sex); (4) details of physical health complication; (5) any comparisons between ARFID and healthy controls (HCs) or AN.

We assessed bias using the Newcastle-Ottawa Scale (NOS) for observational studies, Risk of Bias In Non-randomised Studies for non-randomised studies and Risk of Bias-2 for randomised, controlled studies. We used the CAse REports guidelines for case studies and series for reporting completeness and evidence quality.

Meta-analysis

We pooled studies reporting continuous variables (anthropometric measures and heart rate (HR)) in ARFID compared with HC or AN in meta-analysis when there were three or more studies, using STATA (V.17, StataCorp). Where the same data were reported in more than one paper, we used the most complete sample. For longitudinal studies, we included baseline data.

We generated standardised mean difference (SMD: Hedge's-g) for studies reporting same outcomes but different measures (eg, BMI z-score and %MBMI) and weighted mean difference (WMD) where measures were the same across all studies. We used random effects models due to high heterogeneity between the studies (Q ($p<0.1$) and I^2 (>75%)) and performed meta-regression to examine for potential common study variables moderating effect sizes. We ran sensitivity analyses by removing studies with the highest degree of bias and study outliers based on methodology or study population to examine for impact on effect sizes. We assessed for publication bias with funnel plots and Egger's test for meta-analyses including more than 10 studies.[7]

RESULTS

A summary of search findings is shown in figure 1. Of 9058 studies found in initial searches, we included 132

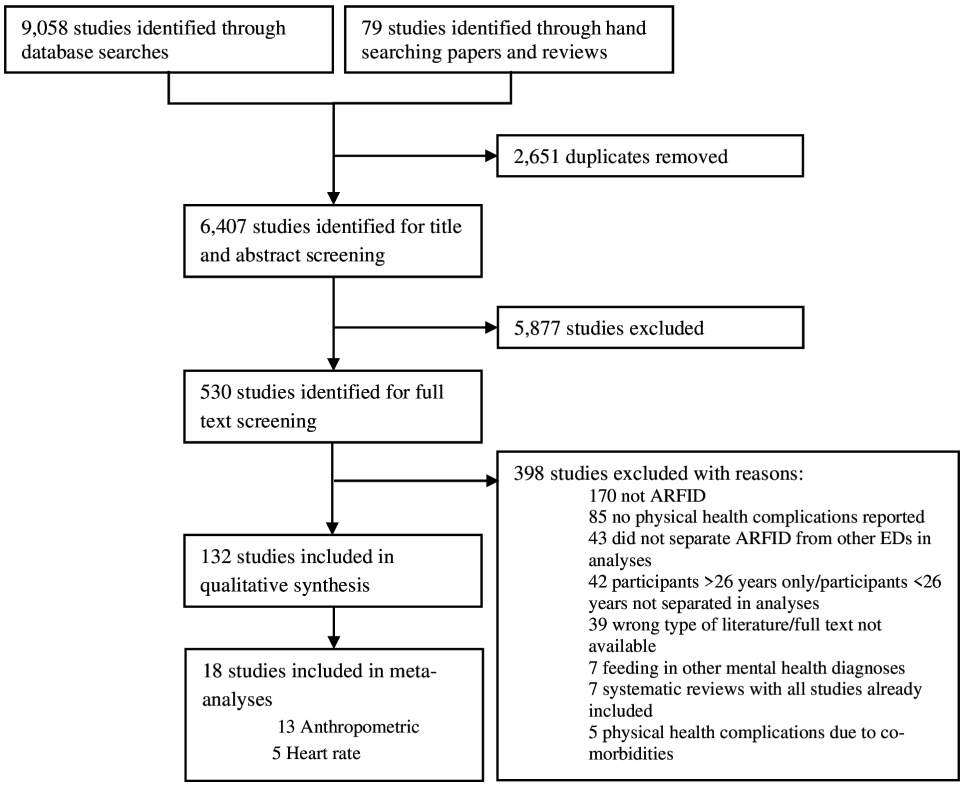

Figure 1 Flow diagram of searches and study selection. ARFID, avoidant restrictive food intake disorder; ED, eating disorder.

studies. All the included studies are described in online supplemental table 1 and referenced in the reference list; however, not all are cited in the text of this paper. Disagreement during the abstract screen was 2.45%. There was no disagreement on the full-text screen. We found studies reporting on the following: anthropometrics (n=128), cardiovascular complications (n=27), BMD (n=12), nutritional deficiencies (n=34), puberty and menstruation (n=13) and other complications that did not fit into the previous categories (n=14). We found 63 cross-sectional studies, 8 longitudinal, 9 research trials (baseline data reported only) and 55 case studies/series. Studies originated from the USA, Canada, Brazil, Japan, Indonesia, Australia, Turkey and Europe. The majority (n=105) of studies were exclusively on children and adolescents ≤18 years, only 15 of which were exclusively on children ≤5 years. The remaining 27 studies were mixed samples of CYP (≤25 years).

Quality of studies

Quality assessments are shown in online supplemental table 1. Median case completeness of case studies was 75% (range: 36%–93%). Median NOS score in observational studies were: case-controls: 6 out of 9* (range: 4–9*); cohorts: 6 out of 9* (range: 4–8*); cross-sectional: 6 out of 10* (range: 4–9*). We also found five out of the nine research trials had moderate risk of bias; the remaining four had high risk of bias.

Anthropometrics

We found 128 studies reporting anthropometric data (online supplemental table 1), including 15 studies which compared HC[8–23] and 28 which compared AN with ARFID.[8–10 14 16 19 23–45]

Seven of the 13 studies reporting weight distribution of CYP with ARFID found the majority were living with underweight (defined within the papers as <5th BMI centile or ≤−2 weight z-score),[15 18 46–50] while six found the majority were within a healthy weight range (defined within the papers as 5th to 85th BMI centile or −2 to 1 weight z-score).[51–56]

We found six studies to pool in meta-analysis comparing BMI z-score or %MBMI in ARFID to HC (figure 2), producing a large overall effect size for lower standardised BMI scores in ARFID (SMD: −0.99; 95% CI: −1.40 to −0.58; n=846)[13–15 18 21 23] compared with HC. Heterogeneity was high (I^2: 79.81%). All pooled studies were in children ≤18 years old, except one study on CYP aged 10–23 years[13] (removal had no significant impact on effect size or heterogeneity). All studies were clinical samples, except one which was a community sample and was the only study of 'poor' quality rather than 'good' quality as assessed by the NOS[21] (removal increased the effect size (SMD: −1.14; 95% CI: −1.46 to −0.82; n=558) and reduced the heterogeneity, I^2: 56.95%.

We also found 15 studies to pool for meta-analysis comparing BMI z-score or %MBMI in ARFID versus AN, producing no overall difference in effect size (SMD: −0.00; 95% CI: −0.31, 0.31; n=1689; figure 3)[9 14 16 19 23 25 27 31 33 34 36 38–40 44]; heterogeneity was high (I^2: 86.57%). Of the 15 studies included, 11 were of children ≤18 years old,[14 16 19 23 25 31 33 34 38 40 44] and the remaining four studies included CYP <25 years of

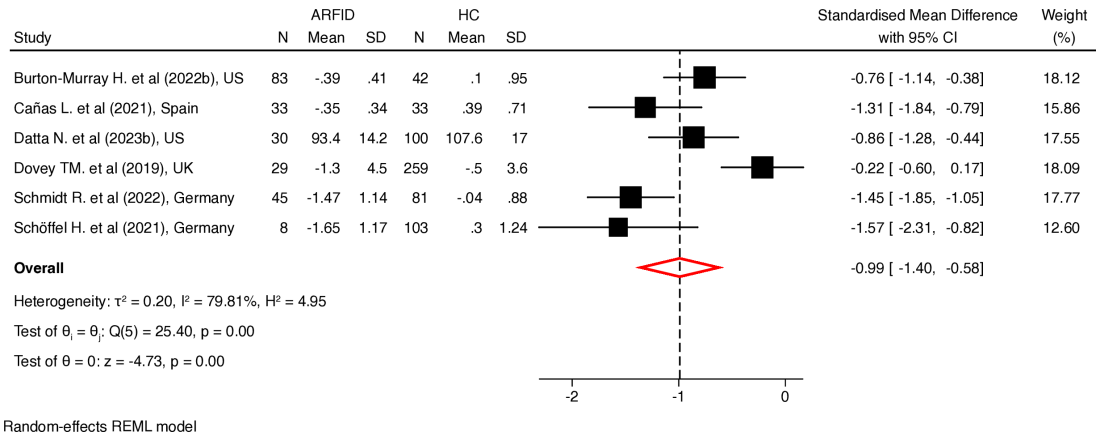

Figure 2 Forest plot showing standardised mean difference in BMI z-scores and %Median BMI between ARFID (n=228) and HC (n=618). 95% CIs and study weights and indicated. The overall effect size was calculated using a random effects model. ARFID, avoidant restrictive food intake disorder; BMI, body mass index; HC, healthy control.

age[9 16 27 36 39] (the removal of which did not affect effect size or heterogeneity). All studies were in clinical samples, except two[16 23] (removal of which did not affect effect size or heterogeneity). Most studies were of 'good' quality; however, six were of 'fair' quality.[19 31 33 38 40 44] Removal of 'fair' quality studies[19 31 33 38 40 44] increased the difference between ARFID and AN; however, SMD was still insignificant (SMD: 0.18; 95% CI: −0.19 to 0.54; n=1004) and heterogeneity was still high (I^2: 82.85%). A funnel plot was not perceived to display asymmetry, confirmed with Egger's test (p=0.64). Meta-regression using available data on age and sex across studies found no significant associations with effect size (data not shown).

Most of the longitudinal anthropometric data we found came from case studies (n=14),[57–70] most reporting rapid weight loss in the months before presentation. We found three larger studies reporting longitudinal data.[39 46 71] One study found that individuals with ARFID had lower pre-diagnosis BMIs and lost significantly less weight during their illness than patients with AN (%MBMI lost: 15% vs 21%; p=0.03).[39] In addition, another study reported individuals with ARFID lost a mean of 9.6±9.1 kg before presentation for treatment.[71] The only study that followed individuals with ARFID for multiple years found that the percentage of them that had severe acute malnutrition (weight z-score ≤−2; from 76% at 2 years of age to 52% at 11 years of age) and those who had severe chronic malnutrition (height z-score ≤−2, 51% to 25%) declined over the years.[46] Five cross-sectional studies mentioned growth faltering or stunting in ARFID; the reported prevalence of growth delay across all five studies ranged from 1.4% to 51%.[46 51 52 54 55]

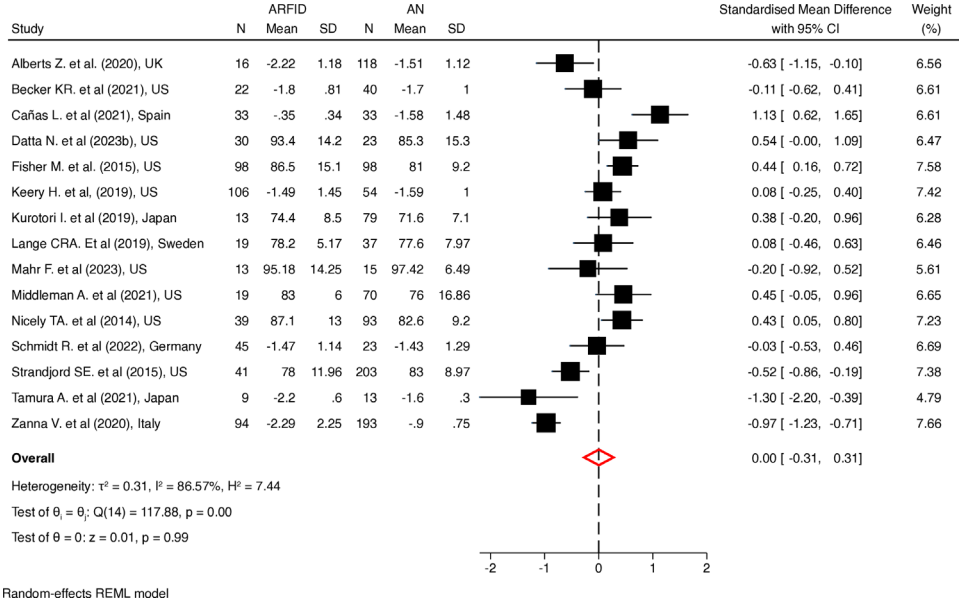

Figure 3 Forest plot showing standardised mean difference in BMI z-scores and %Median BMI between ARFID (n=597) and AN (n=1092). 95% CIs and study weights and indicated. The overall effect size was calculated using a random effects model. AN, anorexia nervosa; ARFID, avoidant restrictive food intake disorder; BMI, body mass index.

Cardiovascular complications

We found 27 studies containing data on cardiovascular parameters in ARFID (online supplemental table 1).[8 19 24 32 33 35 39 41 58 60 61 63 67 70–82] One compared ARFID to HC[8] and seven compared ARFID to AN.[8 19 24 33 35 39 41]

All non-case studies that contained data on HR or blood pressure (BP) in individuals with ARFID found the mean HR and BP to be within a normal range for age.[8 19 24 33 35 41 75 78 82] Several studies did, however, report some individuals with ARFID (3.92%–52.6%) had bradycardia, and around 2% had hypotension.[32 33 39 70 73–75] Five case studies reported tachycardia in ARFID[58 67 72 80 83]; most were reported in the context of electrolyte abnormalities or severe nutritional deficiencies. Two studies investigated potential risk factors for variance in HR and BP within the ARFID population.[75 77] One study identified a subgroup within ARFID that had rapid weight loss and a shorter length of illness also had a lower HR.[77] In contrast, another study found individuals with ARFID who had acute compared with chronic ED symptom onset had similar HRs and BPs (acute: 76.2±15.5 beats per minute (bpm), chronic: 79.4±15.1 bpm, NS).[75] The weight status of the ARFID participants also had no significant impact on their HR or BP, but CYP <12 years had significantly higher HRs (82.40±17.84 bpm vs 76.15±12.23 bpm; p<0.05) and lower systolic blood pressure (109.72±10.14 vs 115.61±8.31; p<0.01) than CYP ≥12 years.

All studies comparing ARFID to AN, reported an average higher HRs, lower prevalence of bradycardia and higher BP in ARFID, despite similar BMIs.[8 19 24 33 35 39] We found five studies to pool in a meta-analysis comparing HR in ARFID to AN, showing that mean HR was greater in ARFID (WMD: 12.93 bpm; 95% CI: 8.65 to 17.21; n=685; figure 4).[8 19 24 33 35] Heterogeneity was high (I^2: 81.33%). All studies included were clinical samples, with two studies of 'good' quality[8 24] and three of 'fair' quality.[19 33 35] Only one study included had CYP over 18 years old (10–22 years old)[8]; removal of which increased the difference in HR between ARFID and AN (WMD: 15.5 bpm; 95% CI: 12.87 to 18.19; n=623). All studies used retrospective medical data apart from two, which were cross-sectional studies[8 35] which when removed increased the mean difference in HR between ARFID and AN to 16.20 bpm (95% CI: 13.28 to 19.13; n=517) and reduced the heterogeneity to null (I^2: 0.00). There was no difference in mean standardised BMI between ARFID and AN in all studies included, except for one[19] were individuals with AN had a lower standardised BMI; removal of which slightly reduced the mean difference and heterogeneity (WMD: 11.69; 95% CI: 7.08 to 16.31; n=398; I^2: 75.91%). Meta-regression and subgroup analysis found no moderators to this relationship (eg, age, percentage female, type of study, year published).

Bone mineral density

We found 12 studies that reported data on BMD within ARFID (online supplemental table 1)[22 24 25 59 84–88]; eight of which were case studies,[59 70 80 81 84–87] one compared BMD in ARFID to HC[22] and two compared BMD in ARFID to AN.[24 25]

In the case studies/series that stated BMD z-score, all individuals with ARFID, except for two,[85 86] had BMD z-scores ≤−2 (BMD z-score range: spine 0.4 to −4.1; hip −3.1 to −4.6).[59 81 85 87] Furthermore, one cross-sectional study reported that 25% of individuals with ARFID had BMD z-scores ≤−2 in their spine while 77% had BMD z-scores ≤−1.[24] Another study found that the mean BMD z-score in individuals with ARFID was −2.46.[88] Only one study mentioned Bone Mineral Density Apparent Density (BMAD) z-scores, where the mean BMAD z-score in individuals with ARFID was −1.44.[25] Lower BMI, lower BMI z-score, amenorrhea and delayed puberty were associated with low BMD.[25] BMI and BMI z-scores were associated with BMAD z-scores. Despite a lower BMI being a risk factor for low BMD, two cases of severe osteoporosis were reported in teenage boys with healthy weight (hip BMD z-scores: −4.1 to −4.6).[59 87]

In the one study that compared BMD z-scores in ARFID to HC, individuals with ARFID had significantly lower BMD z-scores in Total body (−1.41 vs −0.5; p=0.021) and total body less head (−1.67 vs −0.74; p=0.055); however, in the lumbar spine the difference not significant (−0.95 vs −0.67).[22]

Two studies compared BMD z-scores in ARFID to AN. One study found that individuals with ARFID had lower BMD z-scores in their lumbar spine than those with AN

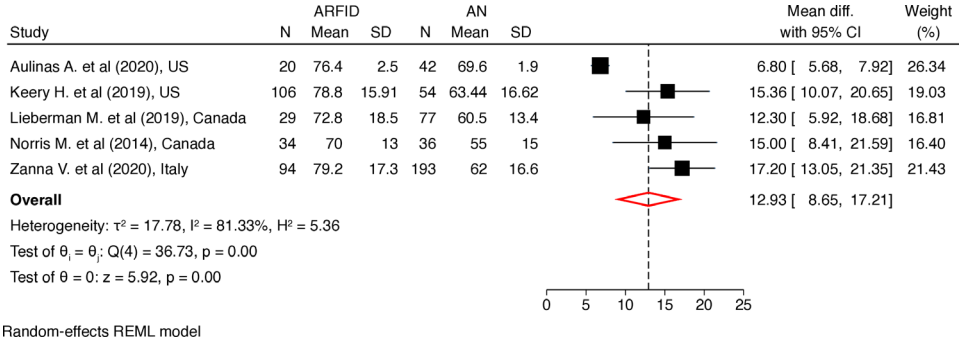

Figure 4 Forest plot showing weighted mean difference in heart rates (beats per minute) between ARFID (n=283) and AN (n=402). 95% CIs and study weights and indicated. The overall effect size was calculated using a random effects model. AN, anorexia nervosa; ARFID, avoidant restrictive food intake disorder.

(−2.00 vs −1.38, ARFID vs AN, p<0.001).[24] Another study reported that although scores were low in both ARFID and AN (−1.88±0.91 and −1.43±1.18, respectively), there was no significant difference between the two.[25]

Nutritional deficiency

We found 34 studies mentioning micronutrient levels in ARFID (online supplemental table 1).[15 43 50 52–54 57–59 69 70 72 80–100] However, only two studies compared dietary nutritional content in ARFID to HC[15 94] and one study to AN.[96]

Five studies contained detailed data on the dietary nutritional content in ARFID; all of which reported a high prevalence of individuals with ARFID not eating the daily recommended intake (DRI) of several micronutrients.[15 52 53 94 96] One study found that 67% of individuals with ARFID consumed <80% of the DRI of six or more micronutrients.[52] Furthermore, our searches identified 22 individuals with ARFID suffering from severe micronutritional deficiencies which led to clinical disorders: xeropthalmia due to vitamin A deficiency[86 87 90 99]; nutritional optic neuropathy due to vitamin B12 and folate deficiency[87 91]; Wernicke encephalopathy due to vitamin B12 deficiency[43]; severe osteoporosis due to vitamin D and/or vitamin B12 deficiencies[59 80 81 84 87]; scurvy due to vitamin C deficiency[52 70 80 84]; pulmonary artery hypertension from vitamin C deficiency[70]; rickets due to vitamin D deficiency[81] and iron deficiency anaemia.[72 80 83 90 91 93 95 97]

In comparison to HC, a higher percentage of individuals with ARFID were not meeting the DRI and were consuming a lower percentage of the DRI in almost all micronutrients tested.[15 94] In contrast, individuals with ARFID consumed less of some micronutrients, such as vitamin C and A, than those with AN but more of others, such as selenium and magnesium.[96]

Puberty and menstruation

We identified 13 studies containing data on puberty and menstruation in ARFID (online supplemental table 1).[8 9 22 29 33 36 38 62 63 67 75 76 101] Six studies compared pubertal and menstrual measurements in ARFID to AN,[8 9 29 33 36 38] and three compared them to HC.[8 9 22]

Amenorrhea (primary and secondary) prevalence was reported at around 10% in females with ARFID.[33 75] Where menstruation data in women with ARFID were compared with those with AN, all studies found significantly more individuals with AN experienced problems with their menstrual cycles, such as a higher prevalence of amenorrhea and more irregular periods, despite similar BMIs.[8 29 33 36]

Pubertal data were reported in three studies; however, all three included participants recruited from the same pool. One study reported that age at menarche in ARFID was older than in HC (13.1 and 12.7 years, respectively); however, this was not statistically significant.[8] In contrast, age at menarche in AN was similar to ARFID (13.2 years). Two of the three studies reported that individuals with ARFID were at significantly lower Tanner stages in breast and pubic hair development than AN and HC.[8 9] However, the individuals with ARFID were significantly younger than the HC, and those with AN. Therefore, the differences in Tanner stage and age at menarche were most likely due to the age difference. In contrast, the final study, which contained individuals with ARFID who were of similar ages to the HCs, found that they were at similar breast and pubic hair tanner stages to those HCs.[22]

Other physical complications

We found 21 studies that reported physical health complications associated with ARFID, which did not fit into the previously described categories (online supplemental table 1).[32 39 58 60 61 67 72–74 97 98 102 103]

The prevalence of electrolyte abnormalities in ARFID was reported to be between 23.1% and 73.7%,[32 39 73] with one study reporting that 23.1% of individuals with ARFID had hypokalaemia and 7.7% had hypophosphatemia.[32] Other electrolyte abnormalities mentioned across studies were hypochloraemia and elevated bicarbonate.[32 58 67 72] Furthermore, in one case of ARFID in a 3-year-old boy, his hypokalaemia was so severe it led to rhabdomyolysis.[58] Another study found that significantly more individuals with ARFID had electrolyte abnormalities than those with AN (23% and 10% respectively, p=0.03).[39]

Several other common physical complications associated with low weight and EDs were reported in ARFID, such as lanugo, lethargy, dizziness, syncope, pale skin, muscle wasting, dehydration, cognitive problems, headaches, hypothermia, diarrhoea and constipation.[60 61 72 76 97 98] One study found that 93 out of 207 (44.9%) CYP with ARFID had one or more of these medical symptoms associated with their ED.[76] Furthermore, some severe, but rare, conditions associated with ARFID, such as Ogilvie's syndrome, hypoalbuminemia and superior mesenteric artery syndrome, were reported by included studies, but the prevalence rates remain unknown.[60 67 72 74]

DISCUSSION

In this systematic review, we have synthesised the current evidence for physical health complications in ARFID, providing important information for clinicians working with CYP with ARFID. We found evidence for several physical health complications commonly associated with undernutrition to be present in ARFID, such as low weight, nutritional deficiencies and low BMD. We found many studies reporting individuals with ARFID at healthy weight or overweight, which is an important observation and highlights that ARFID is not an exclusively low-weight ED, and individuals can present across the weight spectrum. This has important relevance to clinicians, especially where gateways into ED services can be on weight-based criteria.

We pooled studies for meta-analysis to compare weight status between ARFID and HC, and ARFID and AN, and HRs differences between ARFID and AN. However, high levels of heterogeneity in these analyses (I^2: 79.8, 86.6%,

and 81.3%, respectively) introduce complexity and are an important limitation for their interpretation,[104] even though we applied random effects models. The high levels of heterogeneity are not a surprise given that the majority of studies were retrospective, variables extracted were not necessarily primary outcomes and most data came from clinical samples with likely non-standardised approaches to measuring anthropometrics as well as pulse rates (eg, some studies did this using electrocardiograms while others did this manually). That said, in the HR analysis the removal of one study[8] in sensitivity analysis hugely reduced heterogeneity without affecting overall WMD, which is reassuring for the validity of the findings of higher HRs in ARFID versus AN, and remains consistent with all of other studies included in the review. We examined for potential effects on heterogeneity using consistently reported factors such as age and percentage female using meta-regression and found no significance. This all calls for prospective, standardised approaches to measurement of anthropometry and other recognised risk factors, including in clinical settings where important routinely collected data in clinical populations can be collated for analysis.

We found little evidence for the impact of ARFID on growth and puberty, though we would still advocate for monitoring growth and development in CYP with ARFID given the nutritional concerns and the known association between nutrition and growth.[105] Further investigation into the impact on growth, especially longitudinally is needed. We found evidence for micronutrient deficiencies (in some cases associated with very serious complications), electrolyte abnormalities and low BMD in ARFID, all of which did not necessarily discriminate based on the patient's weight (though low BMD was found to be associated with lower BMI status). Some of the most severe cases of micronutrient deficiencies and low BMD were reported in individuals of healthy or overweight status. Therefore, detailed dietetic assessments and physical health assessments should be considered when assessing CYP with ARFID, alongside and irrespective of weight and height measurements.

Most studies of ARFID in CYP reported HRs and BPs to be in normal ranges, (although some did have bradycardia and hypotension) and, as discussed above, our meta-analysis suggests higher HRs in ARFID versus AN in the context of no difference in weight status between participants in included studies. Put together, these are important comparative findings, given the well-known association of starvation in AN and bradycardia.[106] One possible explanation for the greater HR in ARFID versus AN could be that CYP with ARFID tend to be younger than those with AN,[2] and pulse rates are on average are higher at younger ages.[107] That said, in meta-regression we found no association between age or age difference and effect size. In contrast, one study found that the difference in HR between AN and ARFID was no longer significant after correcting for age.[8] We hypothesise that differences in HR between ARFID and AN, despite similar levels of underweight, may be moderated by the often more chronic nature of underweight in ARFID.[108] This is supported by a surveillance study, which reported that CYP with ARFID presenting with more rapid weight loss and a shorter duration of illness were more likely to have a low HR.[77] While we did not find published studies in our searches reporting deaths from ARFID or mortality analyses such as those found for AN,[109] risk of death from malnutrition is very real[109] and ARFID has been reported as cause of death in a child.[110] As we have outlined, ARFID carries the potential for significant and profound physical complications and so here we call for multi-agency vigilance and attention to physical risk. That said, our findings also raise questions about the suitability of using AN exclusively as a model for physical health risk in ARFID,[111] and highlight the need to design risk-based assessment approaches and protocols that are inclusive of all types of EDs.[105] A nuanced and balanced approach to risk in the context of chronicity for when and why to admit in ARFID in relation to weight status would be of value given the common association with neurodevelopmental problems,[112] which themselves are known to carry greater risk for distress and trauma related to hospitalisation.[113]

Our review has strengths and limitations. We used systematic searching by two independent researchers across a broad range of databases. This ensured a wide net to catch all the published studies on any physical health complication in ARFID. Consequently, creating a comprehensive guide to the physical health complications associated with ARFID. Studies included in our meta-analyses were all observational studies and mostly scored similarly in quality assessments. However, we also ran sensitivity analyses, removing the poorest quality studies and study outliers based on samples and methodology. We have already commented on the limitations of high levels of heterogeneity in our meta-analysis. Further to this, a key limitation of our review is that most studies found were small, clinical samples rather than population-based, which may have accounted for the wide prevalence estimates for many physical health complications. We found only five studies on true community samples[17 21 51 55 95] and six from general paediatric clinical settings.[12 18 48 76 77 103] Given the relatively new status of ARFID as a diagnosis, it is perhaps not surprising that many studies are of pragmatic, clinical samples from ED services. However, we emphasise the need for more representative samples, such as population-based studies or at least those seen by General Practitioners or paediatricians, rather than just specialist ED teams. Many of the included studies were also cross-sectional, with few studies identified describing longitudinal changes in physical parameters. This is especially important for understanding the impact on growth and development, with growth faltering being a key consideration in underweight CYP.[114] Therefore, longitudinal studies should be a high priority to investigate ARFID's long- and short-term risks.

In summary, our systematic review has highlighted the broad range of important physical health complications in ARFID, emphasising a need for comprehensive physical health assessments of CYP with ARFID. We have shown that these complications do not always discriminate based on weight, which has implications for gatekeeping access to services based on low-weight cut-offs alone. This review has also highlighted many gaps in the literature regarding the physical impacts of ARFID, particularly a need for more longitudinal growth data. Finally, our review has emphasised important similarities and differences between ARFID and AN, which should be considered in the approach to patients with EDs in the assessment and treatment of physical risk.

Contributors RMJ co-designed the review, wrote the research protocol (and registered with PROSPERO), performed searches, extracted data, performed analyses, and produced the first draft of the paper as part of her PhD thesis. LDH conceived and co-designed the review, supervised screening and data collection, provided adjudication for study inclusion where RMJ and JO disagreed, supervised analyses, supported the first draft, and critically reviewed and revised the manuscript into its final submitted form. JO performed searches, extracted data and contributed to the final paper as submitted. SR and NM co-designed the review, supported the first draft, critically reviewed and revised the manuscript into its final submitted form. All authors contributed to and approved the final manuscript as submitted and agree to be accountable for all aspects of the work. RMJ is the guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; internally peer reviewed.

Data availability statement Data sharing is not applicable to this article as no new data were created in this study, and all analysed data are included in this published article and the supplementary table.

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