THE GLOBAL PREVALENCE OF FOOD SELECTIVITY IN CHILDREN WITH AUTISM SPECTRUM DISORDER: A THREE-LEVEL META-ANALYSIS

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by

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LIST OF SYMBOLS

I^2	Proportion of total variation due to heterogeneity
τ^2	Between-study variance (2LMA)
τ_2^2	Within-study variance
τ_3^2	Between study variance (3LMA)
p	p-value (statistical significance)
k	Number of studies or effect sizes
ρ	Intraclass (intracluster) correlation coefficient; within-study correlation
μ	Overall mean
σ^2	Variance
β	Regression coefficient
Q	Cochran's Q-statistic
df	Degrees of freedom
$\hat{\theta}$	Estimated effect size
v_i	Sampling variance of i estimate
V_j	Working variance-covariance matrix for study j

LIST OF ABBREVIATIONS

ARFID	Avoidant/Restrictive Food Intake Disorder
ASD	Autism Spectrum Disorder
BAMBI	Brief Autism Mealtime Behavior Inventory
BPFAS	Behavioral Pediatrics Feeding Assessment Scale
CHE	Correlated and Hierarchical Effects
CI	Confidence Interval
CR2	Cluster-Robust Variance Estimator, Version 2
DDs	Developmental Disability
FFQ	Food Frequency Questionnaire
FS	Food Selectivity
FS_GEN	General Food Selectivity
JBI	Joanna Briggs Institute
LMIC	Lower Middle-Income Country
LTV	Limited Food Variety
ML	Maximum Likelihood
NEO	Food Neophobia
PE	Picky Eating
PI	Predictive Interval
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
REF	Food Refusal
REML	Restricted Maximum Likelihood

RoB	Risk of Bias
RVE	Robust Variance Estimation
SD	Standard Deviation
SEN	Sensory-Based Food Selectivity
WHO	World Health Organization
YAQ	Youth/Adolescent Questionnaire
3LMA	Three-Level Meta-Analysis
2LMA	Two-Level Meta-Analysis

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PREVALENS GLOBAL SELEKTIVITI MAKANAN DALAM KALANGAN KANAK-KANAK YANG MENGALAMI GANGGUAN SPEKTRUM AUTISME: SATU KAJIAN META-ANALISA TIGA ARAS

ABSTRAK

Keselektifan makanan (Food Selectivity, FS) merupakan isu pemakanan yang lazim dalam kalangan kanak-kanak dengan gangguan spektrum autisme (Autism Spectrum Disorder, ASD), yang ditunjukkan melalui penolakan makanan, pengambilan makanan yang terhad, atau keutamaan terhadap ciri makanan tertentu. Kajian ini bertujuan untuk menganggarkan prevalens keseluruhan global FS dalam kalangan kanak-kanak dengan ASD dan mengenal pasti faktor-faktor yang menyumbang kepada heterogeniti. Kami telah menjalankan ulasan sistematik dan meta-analisis berbilang aras dengan model kesan campuran yang telah didaftarkan lebih awal (PROSPERO ID: CRD4202459844). Carian dijalankan melalui PubMed, Scopus, Web of Science dan ScienceDirect sehingga 22 September 2024. Kajian pemerhatian yang melaporkan anggaran prevalens FS dalam kalangan kanak-kanak dengan ASD berumur 1 hingga 18 tahun telah dimasukkan. Risiko bias dinilai menggunakan Senarai Semak Penilaian Kritikal Joanna Briggs Institute (JBI) untuk Kajian yang Melaporkan Data Prevalens. Sebanyak 18,223 rekod telah dikenal pasti hasil carian pangkalan data. Selepas proses penyingkiran rekod pendua, sejumlah 10,239 rekod unik disaring. Daripada jumlah ini, 315 artikel telah melalui penilaian teks penuh selepas saringan tajuk dan abstrak. Secara keseluruhan, sebanyak 55 kajian yang melibatkan 6,251 peserta dan menghasilkan 144 anggaran prevalens telah dianalisistelah dimasukkan ke dalam analisis. Prevalens terkumpul keseluruhan FS

dalam kalangan kanak-kanak ASD adalah 45.2% (95% CI: 39.5% hingga 51.3%), dengan heterogeniti sisa yang tinggi (I^2 = 94.8%, (Q (143) = 4417.6, $p < 0.001$). Analisis subkumpulan berdasarkan jenis FS menunjukkan perbezaan yang jelas: FS umum mencatatkan prevalens tertinggi pada 59.9% (95% CI: 50.5% hingga 68.5%), diikuti rapat oleh neofobia makanan pada 57.1% (95% CI: 42.8% hingga 70.2%). Kepelbagaian makanan yang terhad dan penolakan makanan menunjukkan prevalens sederhana masing-masing sebanyak 39.3% (95% CI: 29.6% hingga 49.9%) dan 31.7% (95% CI: 15.4% hingga 54.1%), manakala FS berasaskan sensori menunjukkan prevalens paling rendah iaitu 26.0% (95% CI: 18.2% hingga 35.7%). Ujian perbezaan subkumpulan mengesahkan bahawa jenis FS merupakan moderator signifikan kepada variasi prevalens ($p < 0.001$). Walaupun faktor-faktor ini telah diambil kira, heterogeniti sisa dalam subkumpulan jenis FS kekal tinggi (I^2 = 93.2%), menunjukkan kewujudan variasi lain yang tidak dapat dijelaskan sepenuhnya. Analisis berdasarkan wilayah geografi, tahap pendapatan negara, kategori risiko bias, tahun penerbitan, umur purata peserta, saiz sampel dan peratusan peserta lelaki tidak menunjukkan sebarang moderator yang signifikan. Pemilihan makanan memberi kesan kepada hampir separuh daripada kanak-kanak dengan ASD di seluruh dunia, dengan variasi yang besar bergantung kepada jenis FS. Penemuan ini menekankan kepentingan saringan rutin FS dalam kalangan kanak-kanak yang telah disahkan atau sedang disaring bagi ASD.

Kata kunci: Gangguan spektrum autisme, pemilihan makanan, meta-analisis, prevalens, masalah pemakanan

THE GLOBAL PREVALENCE OF FOOD SELECTIVITY IN CHILDREN WITH AUTISM SPECTRUM DISORDER: A THREE-LEVEL META-ANALYSIS

ABSTRACT

Food selectivity (FS) is a common feeding issue among children with autism spectrum disorder (ASD), typically characterised by food refusal, limited dietary variety, or preference for specific food characteristics. A pre-registered systematic review and multilevel meta-analysis (PROSPERO ID: CRD4202459844) using a mixed-effects model was conducted. The objective was to estimate the global pooled prevalence of FS among children with ASD and to explore potential sources of heterogeneity. Comprehensive searches were conducted across PubMed, Scopus, Web of Science, and ScienceDirect database up to 22 September 2024. Observational studies reporting prevalence estimates of FS in children with ASD aged 1–18 years were included. Risk of bias was assessed via Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data. A total of 18,223 records were identified through database searches. After removing duplicates, 10,239 unique records remained, of which 315 full-text reports were assessed following title and abstract screening. Ultimately, 55 studies (including 3 from citation tracking), comprising 144 prevalence estimates, and 6,251 participants were included in the final meta-analysis. The overall pooled prevalence of FS among children with ASD was 45.2% (95% CI: 39.5% to 51.3%), with heterogeneity (I^2 = 94.8%, Q (143) = 4417.6, $p < 0.001$). Subgroup analysis by FS subtype revealed notable variability: general FS exhibited the highest pooled prevalence at 59.9% (95% CI: 50.5% to 68.5%), followed

closely by food neophobia at 57.1% (95% CI: 42.8% to 70.2%). Limited food variety and food refusal were associated with intermediate prevalence estimates of 39.3% (95% CI: 29.6% to 49.9%) and 31.7% (95% CI: 15.4% to 54.1%), respectively, whereas sensory-based FS showed the lowest prevalence at 26.0% (95% CI: 18.2% to 35.7%). A test for subgroup differences confirmed that FS subtype significantly moderated prevalence estimates ($p < 0.001$). Despite accounting for these variables, residual heterogeneity within FS subtype subgroups remained high ($I^2 = 93.2\%$), indicating the presence of further unexplained variation. Moderator analyses revealed no statistically significant effects for geographical region, income level, risk of bias, publication year, mean age, sample size, or proportion of male participants. Food selectivity affects approximately half of children with ASD globally, with substantial variation across subtypes. These findings highlight the importance of routine screening for food selectivity in children diagnosed with ASD or those undergoing assessment for suspected ASD.

Keywords: Autism spectrum disorder, food selectivity, meta-analysis, prevalence, feeding difficulties

CHAPTER 1

INTRODUCTION

1.1 Introduction

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder characterized by persistent deficits in social communication and social interaction across multiple contexts, in addition to restricted, repetitive patterns of behaviour, interests, or activities (American Psychiatric Association, 2022). These behaviours may manifest in various forms, such as hand-flapping, rocking (commonly referred to as "stimming"), repetitive speech, or insistence on sameness in routines and environments (Petitpierre et al., 2021; Tian et al., 2022; Uljarević et al., 2020). These behavioural tendencies may also extend to feeding behaviour, where children with ASD exhibit rigid food preferences, limited food repertoires, and strong resistance to dietary (Petitpierre et al., 2021). The condition manifests early in childhood, typically before the age of three, and persists throughout the lifespan (Hodges et al., 2020). Under the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5-TR), ASD is now considered a single diagnostic category that encompasses previously distinct conditions, such as autistic disorder, Asperger's disorder, and pervasive developmental disorder not otherwise specified (American Psychiatric Association, 2022).

In recent years, the global prevalence of ASD has been increasing, with current estimates suggesting that approximately 1 in 100 children are affected (Maenner et al., 2021; Zeidan et al., 2022). However, the reported prevalence varies significantly across countries and regions due to differences in surveillance systems, diagnostic practices, awareness levels, and cultural contexts. For instance, the prevalence in high-

income countries such as the United States is reported to be over 2.3%, whereas substantially lower estimates have been found in parts of Africa, Southeast Asia, and Latin America, often reflecting underdiagnosis rather than a true difference in incidence (Lord et al., 2022; Zeidan et al., 2022). This rising trend poses substantial challenges to healthcare systems globally, necessitating robust strategies for early detection, diagnosis, intervention, and long-term support for individuals with ASD and their families (Lord et al., 2022; Zwaigenbaum et al., 2015).

Among the many co-occurring issues experienced by children with ASD, feeding difficulties particularly food selectivity (FS) is highly prevalent and frequently overlooked in clinical care pathways (Bandini et al., 2010a; Cermak et al., 2010a). Food selectivity is commonly defined as the consumption of a limited variety of foods, and may manifest as picky eating, strong preferences for specific textures, colours, or food brands, food refusal, or complete avoidance of entire food groups (Bandini et al., 2010; Cermak et al., 2010)). While picky eating is not exclusive to ASD and can be observed in typically developing (TD) children, FS in children with ASD tends to be more persistent, extreme, and resistant to traditional feeding interventions (Sharp et al., 2013). Supporting this, evidence indicates that children with ASD are over five times more likely to experience feeding problems compared to their TD peers, with an odds ratio (OR) of 5.11 (Sharp et al., 2013).

Multiple mechanisms are postulated to contribute to FS in ASD. These include altered sensory processing (e.g., hyperreactivity to taste, smell, or texture), behavioural rigidity, insistence on sameness, limited verbal communication, and emotional dysregulation (Lane et al., 2010; Leekam et al., 2007; Zulkifli et al., 2022). These factors interact to create feeding behaviours that not only limit dietary diversity but

may also cause distress and conflict during mealtimes. Importantly, FS has been associated with a range of adverse health outcomes, including inadequate intake of essential nutrients such as fibre, calcium, iron, and vitamins A and D (Esteban-Figuerola et al., 2021, 2019). Moreover, children with FS may experience altered growth patterns, including underweight, overweight, or stunting, depending on the types of foods consumed and the degree of nutritional imbalance (Raspini et al., 2021; Zulkifli et al., 2022). Gastrointestinal issues such as constipation and reflux are frequently reported among children with ASD and may serve as both contributing factors and consequences of selective eating behaviours (Babinska et al., 2020; Bresciani et al., 2023).

Beyond physical health, the impact of FS extends into psychosocial domains. Families of children with ASD and FS frequently report elevated levels of parental stress, disruption of mealtime routines, and diminished quality of life (Ausderau and Juarez, 2013; Curtin et al., 2015; M. A. Suarez et al., 2014). Feeding difficulties may also impair the development of social and adaptive functioning, given that eating is a culturally significant and socially embedded activity (Ausderau and Juarez, 2013; Rogers et al., 2012; Suarez et al., 2014).

Despite the consequences, FS continue to be underdiagnosed and insufficiently addressed in many clinical settings (Esposito et al., 2023) . One possible reason for this is the lack of standardization in the definition and measurement of FS across research and practice (Zulkifli et al., 2022). This lack of consensus presents a critical barrier to the integration of FS into clinical guideline.

A key challenge is the wide variability in reported prevalence estimates of FS. Some studies suggest that as few as 20% of children with ASD exhibit FS, while others

report rates exceeding 90% (Cermak et al., 2010; Sharp et al., 2018; Wenzell et al., 2024). These disparities are likely due to methodological heterogeneity, including differences in sample characteristics (e.g., age, cognitive functioning), recruitment settings (e.g., clinical vs. community), geographical and cultural contexts, and operational definitions of FS (Zulkifli et al., 2022). Furthermore, many studies report multiple effect sizes for different subgroups (Alkhalidy et al., 2021; Zhu et al., 2020) , age ranges (Gray and Chiang, 2017), or FS dimensions (Bandini et al., 2016; Provost et al., 2010) ,which introduces statistical dependency and violates the assumption of independence in conventional meta-analytic models (Abbas-Aghababazadeh et al., 2023; Hedges and Schauer, 2019).

From a public health and epidemiology perspective, generating a precise and generalizable estimate of FS prevalence is essential for guiding resource allocation, informing dietary interventions, and shaping caregiver education programs (Binns et al., 2017; Grosse et al., 2007). Identifying key moderators that influence prevalence such as child age, region, socioeconomic status, or diagnostic tools may reveal important disparities and inform targeted approaches to care (Bandini et al., 2016; Schreck and Williams, 2006; Zulkifli et al., 2022). Additionally, accurate prevalence estimates serve as baseline data for health economics modelling and intervention trials (Briggs, 2006; Drummond, 2015).

Meta-analysis plays a crucial role in synthesising disparate prevalence estimates from individual studies to generate a pooled estimate that reflects the overall burden of FS among children with ASD (Borenstein et al., 2010, 2009). This approach allows for increased statistical power, enhanced precision, and the ability to explore sources of heterogeneity through moderator analyses. However, many of these earlier

syntheses were narrative in nature or relied on simple meta-analytic techniques that did not account for the hierarchical structure of the data or the presence of multiple estimates per study (Esteban-Figuerola et al., 2019; Sharp et al., 2013; Zulkifli et al., 2022). As a result, their findings may be biased or less precise, underscoring the need for more advanced quantitative methods (Tanner-Smith et al., 2016; Tanner-Smith and Tipton, 2014).

Traditional meta-analytic methods, which assume independence among effect sizes, are ill-suited for synthesizing complex data structures that involve multiple effect sizes nested within studies (Borenstein et al., 2010, 2009; Cheung, 2019; Park and Beretvas, 2019). This is particularly problematic when studies report estimates for multiple subgroups or timepoints, a common feature in the FS-ASD literature (Harrer, 2021). To address this, three-level meta-analysis (3LMA) has emerged as a statistically robust method that accounts for dependencies by partitioning variance across three levels: sampling variance (level 1), within-study variance (level 2), and between-study variance (level 3) (Assink and Wibbelink, 2016; Harrer, 2021).

Additionally, recent advances in meta-analytic methodology have introduced robust variance estimation (RVE) techniques such as the Clustered Heteroskedasticity Estimator (CHE) and Cluster-Robust Variance Estimator, Version 2 which further correct for model misspecification and heterogeneity in effect size precision (Pustejovsky and Tipton, 2018). These methods allow for valid inference even in the presence of complex within-study correlation structures and small numbers of clusters.

In this thesis, a three-level meta-analysis was conducted to estimate the pooled global prevalence of FS among children with ASD, integrating robust statistical estimators to address methodological challenges in the literature. The results aim to

provide a nuanced and statistically rigorous understanding of the prevalence of FS in ASD, serving both clinical and policy-making objectives. By leveraging advanced meta-analytic tools, this work seeks to bridge the gap between disparate findings and deliver meaningful insights that can improve nutritional care, intervention planning, and health outcomes for children with ASD worldwide.

1.2 Problem Statement

Despite growing awareness of FS as a prevalent and clinically significant concern among children with ASD, the current evidence base is characterised by substantial fragmentation and methodological inconsistencies. Prevalence estimates vary widely across studies which reflects heterogeneity in the operational definitions of FS, assessment tools used, sample characteristics, and study settings (Cermak et al., 2010; Sharp et al., 2018, 2013; Wenzell et al., 2024; Zulkifli et al., 2022). Such variability limits comparability across studies and complicates the ability to draw definitive conclusions regarding the true burden of FS.

A critical methodological gap in the literature is the absence of standardisation in defining and measuring FS (Zulkifli et al., 2022). Studies have employed diverse instruments ranging from unvalidated parent-report questionnaires to structured clinical observations, each with varying degrees of reliability and validity (Cermak et al., 2010a; Esposito et al., 2023; Hubbard et al., 2014; Marí-Bauset et al., 2014). This inconsistency undermines efforts to synthesise findings and develop unified diagnostic criteria or clinical guidelines. Additionally, studies often report multiple prevalence estimates within the same cohort, stratified by age group, FS subtype, or comorbidities. The statistical dependency introduced by such data structures violates assumptions of