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The application of population data linkage to capture sibling health outcomes among children and young adults with neurodevelopmental conditions. A scoping review

Caitlin Gray[1,2*], Helen Leonard[2,3], Matthew N. Cooper[2], Dheeraj Rai[4,5], and Emma J. Glasson[2,3]

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[1] Paediatrics, Medical School, The University of Western Australia, Perth, Australia
[2] The Kids Research Institute Australia, Centre for Child Health Research, The University of Western Australia, Perth, Australia
[3] Discipline of Psychiatry, Medical School, The University of Western Australia, Perth, Australia
[4] Population Health Sciences, Bristol Medical School, Bristol, United Kingdom
[5] Avon and Wiltshire Partnership, NHS Mental Health Trust, United Kingdom

Abstract

Introduction
Siblings of children with neurodevelopmental conditions have unique experiences and challenges related to their sibling role. Some develop mental health concerns as measured by self-reported surveys or parent report. Few data are available at the population level, owing to difficulties capturing wide-scale health data for siblings. Data linkage is a technique that can facilitate such research.

Objective
To explore the application of population data linkage as a research method to capture health outcomes of siblings of children with neurodevelopmental conditions.

Inclusion criteria
Peer reviewed papers that captured health outcomes for siblings of children and young adults with neurodevelopmental conditions using population data linkage.

Methods
JBI Scoping review methods were followed. Papers were searched within CINAHL, Ovid, Scopus, and Web of Science from 2000 to 2024 using search terms relating to 'data linkage' 'neurodevelopmental conditions' 'siblings' and 'health outcomes'.

Results
The final data extraction included 31 papers. The neurodevelopmental conditions of index children were autism, attention deficit hyperactivity disorder, intellectual disability, cerebral palsy and developmental delay. The mean follow-up time was 31 years, and the majority of studies originated from Scandinavia. Sibling health outcomes observed were psychiatric diagnoses, self-harm and suicide, other neurodevelopmental conditions, and medical conditions such as atopic disease, cancer and obesity.

Conclusion
Data linkage can help capture sibling health outcomes quickly across large cohorts with a range of neurodevelopmental conditions. Future research could be enhanced by focusing on siblings as the primary group of interest, increased integration of genealogical data, and comparisons between diagnostic groups and severity levels. Adoption of established rigorous reporting methods will increase the replicability of this type of research, and provide a stronger evidence-base from which to inform sibling supports.

Keywords
Neurodevelopment; siblings; data linkage; population-level; health outcomes; scoping review

*Corresponding Author:
Email Address: Caitlin.Gray@thekids.org.au (Caitlin Gray)

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Introduction

Neurodevelopmental conditions (including intellectual disability, autism, cerebral palsy, attention deficit hyperactivity disorder, and some genetic syndromes) are usually diagnosed in childhood, and are associated with varying levels of support needs [1–3]. Siblings of children with these conditions can provide important companionship and care, sometimes having informal carer roles as children and more formal care roles as adults [4–7]. Siblings are often described as having positive character traits, and develop rich relationships as a result of growing up alongside someone with a disability [8, 9], yet some may also be at risk of poorer health outcomes compared to their peers, which may be the result of shared genetics, environmental factors, family factors, or a combination of these [10–12]. Neurocognitive difficulties, psychiatric diagnoses, and self-harm have been observed in some siblings during childhood and young adulthood [13–17].

Health outcomes for siblings are often reported at the individual level, using interviews [18–20] or surveys [21, 22], and are sometimes subject to convenience sampling of available siblings or families of children who have specific neurodevelopmental conditions [23, 24]. The evidence base around the health outcomes of siblings at a population level is relatively sparse. Compared to surveys and clinical samples, population-based data can help obtain adequate sibling sample sizes and representation for minority groups and rare conditions [25–31]. Population data also allow the selection of comparison groups from the same time period and data collection parameters, which strengthens the context and interpretation of the findings. Further, it can also reduce the need for follow-up if enough data are available. Existing data minimises recall bias, attrition, or limitations on resources to engage participants, that can occur when collecting data from individuals directly [32].

Population data relating to individuals with neurodevelopmental conditions are usually collected and maintained in specific administrative databases [33–36], or in disability-specific population databases [26, 37–40], and these rarely include data on other family members. Using data linkage methodologies, disability data can be connected to health and other datasets, including genealogical connections, to follow individuals or families across wide-ranging domains. Linkage allows for large-scale analyses to occur for specific sibling health outcomes and wellbeing trajectories, and provides a unique evidence-base from linking together information that would otherwise remain siloed or fragmented [32, 41–43]. The use of high quality linkage methods and databases can minimise linkage error bias that can occur when linking population data [44].

The benefits of applying data linkage to independent data sources for sibling research are significant [45, 46]. Linkage can update or extend existing data repositories and can rapidly merge relevant information for faster interpretation and response, especially important for mental health concerns. Life course experiences of siblings can be tracked [47] across a wide variety of contacts with health (e.g. hospital visits, medication prescriptions, mental health contacts) or other registries (e.g. education, census data, crime) until the end of the follow up period, or death [28, 41]. Data linkage can be used to improve visibility of siblings of individuals with rarer neurodevelopmental conditions for whom understanding health patterns and circumstances may require data extensions beyond a single administrative system. The data linkage process itself is able to preserve confidentiality [48] and reduces the need to approach individuals to collect information that may already exist, or be difficult to collect.

The objective of this scoping review was to explore the application of population data linkage as a research method to capture health outcomes of siblings of children and young adults with neurodevelopmental conditions, and ways data linkage can enhance knowledge in this field. This review describes the population characteristics and methodology of studies meeting the eligibility criteria, the neurodevelopmental conditions of index children, sibling health outcomes reported, and the infrastructure used.

Before commencement, scoping review databases (Open Science Framework, Figshare, JBI Evidence Synthesis, and BMJ Open) were searched for similar registered reviews, but no protocols involving the key terms for this review were identified.

Review questions

What are the characteristics of population data linkage studies that capture health outcomes of siblings of children and young adults with neurodevelopmental conditions?

How has population data linkage been used in these studies to capture health outcomes that originate in childhood or young adulthood, what are the capabilities of data linkage to explore wide scale health outcomes for siblings, and what could be enhanced to improve future sibling research involving linked data?

Inclusion criteria

Studies using population data linkage (administrative data, registry data, and research databases) in a defined geographical area (a country, state or territory, or region bounded by government or administration) to capture health outcomes (physical and/or mental health) of siblings of children and young adults with neurodevelopmental conditions were considered. All study designs were included e.g. quantitative, population based, longitudinal or cohort studies, if they met the inclusion criteria.

Studies were included if both index children with neurodevelopmental conditions and their siblings were children or young adults, defined as being aged up to 25 years [49]. Siblings did not need to be the primary group of interest as long as sibling data (full or half siblings) were presented. In studies where sibling ages were not stated or were combined with cases/controls, the estimated mean age for index children could not exceed 25 years. Twin studies were included if twins were identifiable in subgroups, and if other singleton sibling data were available. Where possible, comparators comprising of siblings of children and young adults without neurodevelopmental conditions were included.

The neurodevelopmental conditions of index children must have been diagnosed clinically and/or recorded as an entry in either a population administrative dataset(s), diagnosis

specific registry or project database using standardised classification systems (e.g. Diagnostic and Statistical Manual of Mental Disorders (DSM) [50], International Classification of Diseases (ICD) [51]). For example, identification of a diagnosis of intellectual disability using DSM in a disability specific registry, a record of autism using an ICD code in registry-based patient records, or identification of attention deficit hyperactivity disorder using a medication code in a prescribed drug registry.

Sibling health outcomes captured must have been presented as clinical diagnoses and recorded as a standardised entry in a relevant database. For example, identification of a diagnosis of obesity using a record of ICD code in registry-based hospital records, or a record of death using a cause of death code in a mortality registry. No inclusion criteria were applied to social, cultural and gender constructs.

Methods

This scoping review followed the JBI methodology for scoping reviews [52], and a JBI checklist was completed as an assessment of conformity [53]. A protocol was published a priori in Open Science Framework [54] which outlined the objectives, inclusion criteria, and methods planned [55].

Search strategy

The search strategy was developed in consultation with a subject specialist librarian. The following databases were searched: CINAHL, Ovid (MEDLINE, Embase, PsycINFO), Scopus, and Web of Science. All search terms belonged to one of four categories: data linkage, neurodevelopmental conditions, siblings, and health outcomes (Supplementary Material 1). Papers were excluded if they were: published before the year 2000; without abstracts/full text; from non-peer reviewed sources; or in grey literature (e.g. theses). The search was performed for papers published between 1st January 2000 and 1st October 2024. The search returned 9,753 matches.

Source of evidence screening and selection

Records were imported into Endnote and duplicates were deleted (n = 4,098). The SR-Accelerator (SRA) suite of automated tools [56] was used to facilitate the screening and selection process. The Screenatron function was used to screen all records at the title/abstract level and the full-text level. The Disputatron function was used to identify areas of inconsistencies between reviewers.

Step 1 (Title/abstract level): Titles and abstracts for all included records (n = 5,655) were independently screened by two reviewers (CG and EG) using Screenatron. Records were then marked as 'include' or 'exclude' by each reviewer. In cases where the reviewers were unsure, records were marked 'include'. The lists of both reviewers were then imported into Disputatron to identify reviewer inconsistencies. In cases where the reviewers disagreed, records were marked 'include' for screening at the next level. Full-texts for all included records were obtained through databases, online, or requests from other institutions/authors.

Step 2 (Full-text level): Eligible full-text papers (n = 285) were independently screened by CG and EG using Screenatron and Disputatron (as per Step 1). In cases where the reviewers disagreed, papers were discussed, and in all cases, agreement was met.

Step 3 (References level): Reference lists of all included papers (n = 31) were manually screened by CG for additional papers not identified in the initial search. Additionally, the linked data reference library of the Population Health Research Network (PHRN) [57] was manually screened by CG. There were no additional papers identified at this level.

Papers were excluded when: data relating to siblings were not captured; there were no identifiable neurodevelopmental conditions among index children; non-standardised measures were used instead of diagnostic standardised classification systems (e.g. self/parent-report, survey responses and scales); the neurodevelopmental conditions among index children (e.g. autism) were the same as the sibling outcome observed (i.e. autism), such as recurrence risk studies; there were no linkages to other external data; the direction of the study design was retrospective, e.g. a sibling outcome such as obesity was identified first, then followed back to investigate the neurodevelopmental condition status of index children (e.g. autism); they were other reviews (systematic, scoping, literature etc.).

Data extraction

Data on methodology and results were extracted from papers by one reviewer (CG), using a customised form created by two reviewers (CG & EG) (Supplementary Material 2), and over a quarter were cross checked by a second reviewer (EG). The form was updated as the extraction was performed. Extracted data fields included information about each paper's aim in relation to the sibling data captured, type of neurodevelopmental condition of index children, sibling health outcomes captured, age range, population source, databases used, sample size and follow-up times.

Analysis and presentation of results

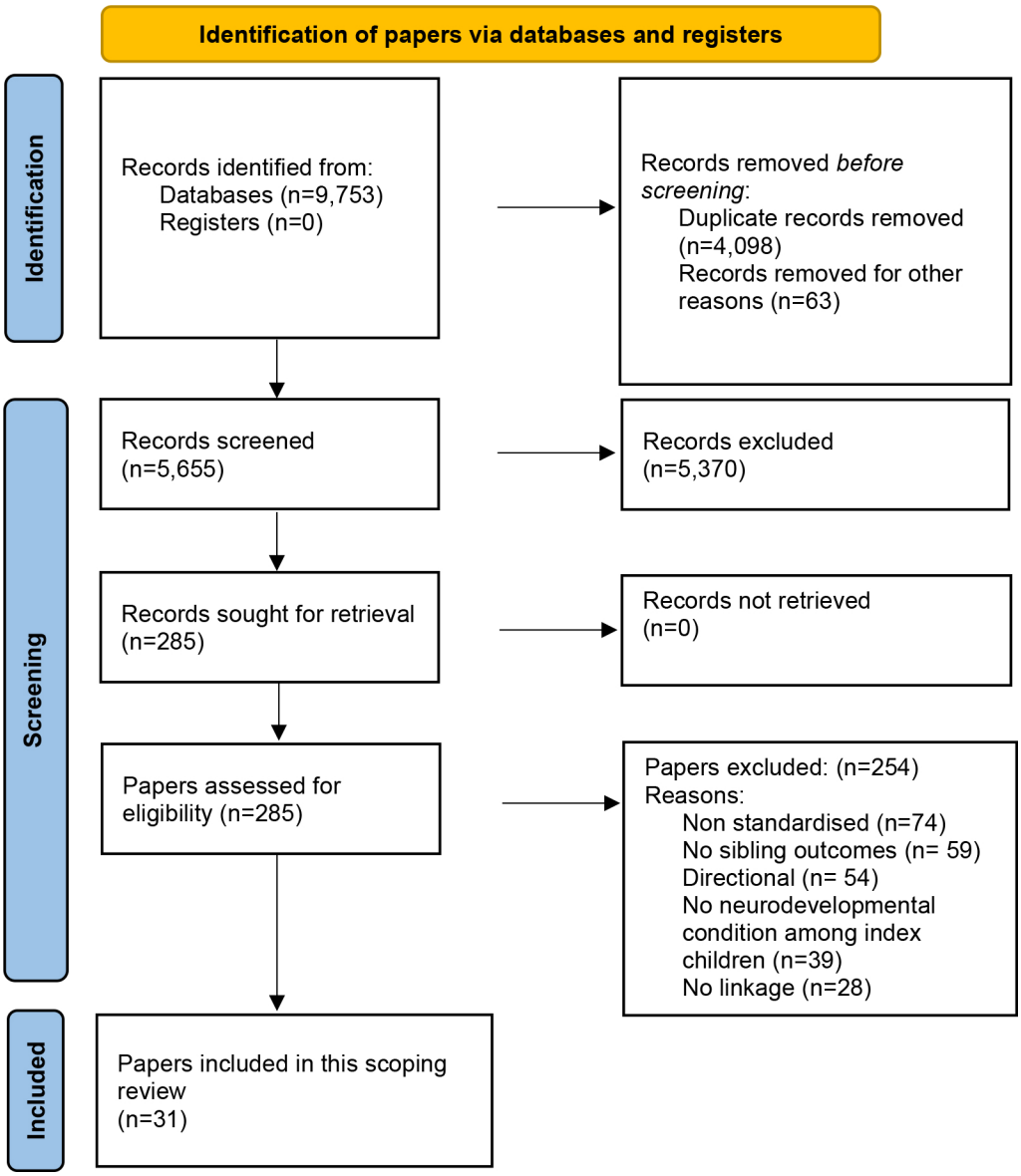
This scoping review identified, mapped, and summarised publicly available sources of population data linkage research capturing sibling health outcomes of children and young adults with neurodevelopmental conditions. The findings are presented in an extraction table and supported by a descriptive summary of the findings that emerged iteratively through the extraction process.

Results

The identification and inclusion of papers were made according to the guidelines of Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping reviews (PRISMA-Scr) [53] (Figure 1). A total of 31 papers met the criteria for inclusion.

CINAHL, Ovid (MEDLINE, Embase, PsycINFO), Scopus, and Web of Science were the final search sources of evidence for papers that captured sibling health outcomes of children and young adults with neurodevelopmental conditions using

Figure 1: PRISMA-Scr flow diagram [58]



data linkage methods. Papers were published in a variety of journals, most of which related to the neurodevelopmental condition of index children or sibling health outcome observed (e.g. papers capturing data on psychiatric disorders were published in psychiatric journals). Some journals had a broader focus (e.g. paediatrics, open medical journals), and a few journals related to population-based methodology (e.g. epidemiology, population health) [59, 60]. A summary of paper characteristics of the final sources of evidence are reported in the Summary table (Table 1). The full results of this scoping review are reported in the Data extraction table (Supplementary Material 3). The following findings are presented as a descriptive summary of the paper characteristics, methodologies, neurodevelopmental condition of index children, and sibling health outcomes presented.

Print publication dates of included papers ranged from 2013 to 2024, most of these since 2019 (Table 1). Many papers referenced familial or first-degree relatives in the title and included siblings within this broad category (Table 1) [61–64]. Around one third of papers referenced siblings in the title of the paper [65–67], and in most of these, siblings were the primary interest group. The remainder of papers had no reference to siblings or family in the title [68–70]; however, sibling data were included in the abstract and body of the papers.

The majority of papers related to studies from Norden countries. The total papers were represented by the following countries in order of Sweden, Taiwan, Finland, Norway, Denmark, and Canada (Table 1). Thirty-nine unique datasets were used for data linkage across all included studies, of which 20 were databases used in the 20 Swedish studies (Supplementary Material 3). On average, each paper reported on data from five linked datasets, up to 11 in some instances. The most commonly reported datasets were those relating to births, family connections, hospital, medication, health insurance, and deaths.

Half of the included papers reported a whole population study design, and the remainder a matched case-control study design (ratios ranged from 1:4 to 1:50 matched controls) (Table 1). Sibling cohort size for whole population studies ranged from 3,410 to 4,289,186, with a mean of 1,270,764 individuals (Table 1). As expected, sibling population sizes were smaller among matched control designs, ranging from

Table 1: Summary table

Paper characteristics	**n = 31**	**%**
Geographic location		
Sweden	20	64
Taiwan	6	19
Finland	2	7
Norway	1	3
Denmark	1	3
Canada	1	3
Publication year		
>2020	11	35
2017-2020	13	42
2013-2016	7	22
Neurodevelopmental condition of focus		
Autism	16	52
Attention deficit hyperactivity disorder	10	32
Intellectual disability	3	10
Cerebral palsy	1	3
Developmental delay	1	3
Sibling outcome		
Psychiatric/mental health	17	55
Neurodevelopmental	5	16
Physical health	9	29
Birth year (earliest)		
>1989	2	6
1980-1989	10	32
1970-1979	9	29
1960-1969	2	6
<1960	1	3
Missing	*7*	*22*
Age range (years)		
>39	1	3
30-39	6	19
20-29	6	19
10-19	4	13
<10	3	10
Missing	*11*	*35*
Follow up time (years)		
>30	12	39
20-30	3	10
<20	6	19
Missing	*10*	*32*
Number of registries		
>7	5	16
5–7	12	39
<5	14	45
Study design		
Whole	16	52
Matched	15	48
1:50	*3*	*20*
1:10	*3*	*20*
1:5	*2*	*13*
1:4	*7*	*47*
Sibling population size		
>999,000	4	13
100,000-999,000	5	16

Continued

Table 1: Continued

Paper characteristics		n = 31	%
	<100,000	15	48
	Missing	*7*	*23*
Title references to siblings			
	Siblings	11	35
	Family	12	39
	Neither	8	26
Sibling characteristics			
	Birth order	6	19
	Sibling size	5	16
	Both	2	6
	Missing	*18*	*58*
Sibling focus			
	Primary group of interest	9	29
	Comparison group	22	71

1,304 to 665,994, with a mean of 82,793 individuals. One third of included papers reported on paternal and maternal half siblings, in addition to full siblings. Almost half of all papers reported sibling characteristics such as birth order and/or sibling size.

Across all papers, duration of follow-up ranged from 15 to 77 years with a mean of 31 years, and sibling ages ranged from 0 to 44 years (Table 1). Cohort birth years ranged from 1932 to 2013, with around one-third of studies having birth years beginning between 1980 to 1989.

Siblings were the primary group of interest in almost one third of papers, while the remaining two-thirds of papers included sibling data for comparison to the index cases and/or controls (Table 1). Each paper's aim has been provided in relation to the sibling data captured within the paper (Supplementary Material 3).

The neurodevelopmental conditions of index children included autism, attention deficit hyperactivity disorder, intellectual disability, cerebral palsy, and developmental delay (Table 1). Most studies on autism included subgrouping for the presence of intellectual disability [71], and over half captured sibling outcomes for these subgroups [72, 73]. Two studies on intellectual disability included subgrouping by severity levels, and one of these reported sibling outcomes for the subgroups (Supplementary Material 3) [74].

Sibling health outcomes captured were wide ranging, from broad outcome categories to specific conditions (Supplementary Material 3) [64, 75–79]. The most common were psychiatric or mental health conditions, followed by physical health conditions, and neurodevelopmental conditions (Table 1).

Discussion

Findings from this review demonstrate the utility of population data linkage to capture health outcomes of siblings of children and young adults with neurodevelopmental conditions, including when siblings are not the primary focus. The sibling data captured in the reviewed papers, and the final number of included papers, was shaped by the data linkage capabilities in the area where the research was being conducted, and therefore narrowed the findings accordingly. Despite this, the search was able to generate an informative understanding of the application of data linkage as a method to deliver population perspective in this field. The included papers demonstrated a wide scope in target populations and sample sizes, a range of diagnostic observations, and availability of sibling data spanning decades of data collection. These qualities have significant benefits for sibling research by facilitating the exploration of sibling wellbeing in adequate samples across disability types, developmental ages and a broad range of outcomes, allowing representation of siblings in a variety of contexts.

Recent increases in the number of eligible papers indicates a general growth in sibling-based research. The countries represented in this scoping review reflects the availability of population data infrastructure and capabilities in those regions, the linkages that readily occur between datasets, and locations where genealogical connections may be more available [80–84]. Sweden, for example, has established two population registers, the population register (maintained by the Swedish National tax agency), and the Total Population Register (TPR) (maintained by the government agency Statistics Sweden). Both registers contain large amounts of health and other data, and family links, and updates are transmitted daily [81]. Whereas, in Taiwan, a data repository site, the Health and Welfare Data Science Center (HWDC), was established to centralise the National Health Insurance Research Database (NHIRD) and around 70 other health databases, to streamline research data management [82]. The power of data aggregation from both types of infrastructure is significant, and combined with the availability of family linkages resulted in the inclusion of many papers into this review. The absence of papers from other geographical areas with established data infrastructure and linkage capabilities [85, 86] reflect capability or methodological differences that prevented their inclusion in the current review, and highlights avenues for future research in this field to be explored.

The types of registries used in the included studies varied, depending on the diagnostic groups of index children, sibling health outcomes observed, and the availability and suitability of data sources [87]. Many studies used government registries e.g. birth registers, which support broad population data collection and increase the feasibility to conduct linkage to other datasets. The use of longitudinal government-maintained statutory databases assumes a consistency and quality of data and data linkage methods, providing confidence to the findings of studies that use these resources. Studies typically linked multiple registries, demonstrating the versatility and broad application of data linkage methods for sibling research, where data may need to be captured across different domains. This allows considerable power and breadth in the types of analyses that can be made at the population level, and demonstrates the benefits of combining data from sources that would otherwise remain independent [88, 89].

The majority of studies used ICD codes extracted from government-based records (e.g. hospital, prescription, or mortality databases) to identify diagnostic groups and/or outcomes [81, 82], enhancing consistency and replication of the studies. However, validation issues surrounding adequate identification of neurodevelopmental conditions such as intellectual disability in these databases have been raised and should be acknowledged [90]. Other studies used DSM classification systems to identify diagnostic groups and/or outcomes, which may be partial to similar limitations. In addition, diagnostic trends and the ability to co-diagnose some neurodevelopmental conditions (e.g. autism and attention deficit hyperactivity disorder [91]) have evolved over time, and comparability across a long time period may be limited. Knowledge has also increased of the presentation of some conditions, such as attention deficit hyperactivity disorder in individuals with a learning or intellectual disability [92], or autism in females [93], which may also impact on comparisons across different studies or time cohorts. It also warrants caution in using coded data for inferring genetic risk. In this review, studies often used non-government registries (i.e. Stockholm youth cohort, psychiatric registers), which typically housed data dedicated to specific conditions, not purely for administrative purposes [94]. Such registries can provide unique data and perspective, greater diagnostic accuracy, inclusion of rarer conditions, and finer details such as severity level, which are vital to assessing sibling outcomes [14, 95]. However, for condition-specific registries, availability of family links may not be possible or sustainable due to the resources required to build and maintain them. Resources devoted to developing these data sources, and enhancing linkage capabilities between government-based datasets and disability specific/non-government datasets would help improve the availability of data capture in the future.

The lengthy follow-up times of the included studies highlight a significant benefit of using linked data for sibling research, enabling longitudinal data analyses, spanning different developmental and life stages within a relatively short analytical timeframe. In contrast, establishing a prospective study to collect equivalent data would require sustained data collection and resources over the entire follow up period. It is vital to consider life-course approaches to sibling mental health, as many siblings adopt formal carer roles later in life, and experience challenges as adults [96], but for some, mental health concerns are already observed in childhood [21]. Data linkage allows the analysis of health and wellbeing indicators from birth to understand trajectories of development and change, covering boundaries of childhood, where siblings live with their families, to early adulthood where independence is reached, and formal caregiving may occur within the enduring sibling relationship. Data linkage allows bridging of childhood and young adulthood data with health outcomes observed later in adulthood to support a lifespan approach to monitoring and improving sibling wellbeing.

The length of exposure, based on the youngest age at which outcome conditions were diagnosed in siblings, can be used to determine at what ages sibling supports are most needed [25, 45, 83]. Some studies in this review used a narrow age range, e.g. nine calendar years, and reported specific sibling outcomes for that age period [97, 98], showcasing more precise capabilities of data linkage methods. However, the majority of studies grouped sibling data, regardless of age and length of follow up, sometimes spanning 77 years [75], thereby limiting the interpretation by sibling age due to the lengthy time periods of mixed-age data aggregation. The use of linked longitudinal population data to advocate for sibling supports at more specific life stages is an important capability, and is a recommended focus in future work.

Reliable integration of genealogical data can be difficult to incorporate at scale using other non-linkage-based study designs. The papers in this review all used population-based genealogy to establish sibling relationships (full siblings, maternal/paternal half siblings etc.), of up to 4.3 million individuals in the largest sample [42]. Sibling characteristics such as sibling size, spacing and birth order are considered important risk or protective factors for various health outcomes [99, 100] and reporting of these characteristics is readily facilitated by linked population data. In this review, some papers included frequencies of sibling characteristics as demographic content [67, 68, 76, 101–103], while others included sibling characteristics as covariates to control for confounding effects [104], often combined with other socio-economic variables, thus limiting the context of the findings for siblings. In papers that reported these characteristics more comprehensively, additional benefits of population data for sibling outcomes were demonstrated [60, 79]. For example, presenting outcome rates based on the sex of the sibling, sibling size, and age distance to the index child [60], and using birth order to define sibling dyads and degree of risk [79]. Incorporating and reporting detailed sibling characteristics allows a greater understanding of how sibling relationships and family environments shape their outcomes across multiple domains.

Siblings can have unique life experiences, often shaped by the type and severity of neurodevelopmental conditions among children in the family [9]. Study designs that allow for comparisons to be made between condition types and severity levels can provide greater accuracy about sibling experiences and outcomes. Data linkage methodologies can facilitate this design, particularly for rare or lower prevalence conditions, and the ability to link to registries containing finer diagnostic detail. All papers in this review focused on index children with the same neurodevelopmental condition, thus limiting the ability to compare outcomes between different diagnostic groups in the one study design. One paper that focused

on intellectual disability, reported outcomes for different intellectual disability severity levels, allowing enhanced sibling data to be captured, for example, showing stronger sibling risk of attention deficit hyperactivity disorder for mild and moderate intellectual disability than for severe intellectual disability [74]. Most papers did not report results by level of intellectual disability, citing potential overlapping genetic risk for neurodevelopmental conditions [105, 106] or the lower prevalence levels in intellectual disability subgroups [94], it may also be due to inadequate identification of intellectual disability in the databases used [90]. Studies including index children with autism, often subgrouped by the presence or absence of intellectual disability, reflecting the recognised independent effects of both autism and intellectual disability on outcomes [102, 107–109]. Studies where sibling data can be captured for different severity levels allow interpretation of the impact these differences may have on sibling health outcomes, and consequentially, understanding how to best support siblings according to their family circumstances.

The neurodevelopmental conditions of index children and sibling outcomes among studies included in this scoping review reflected population prevalence and publication trends, whereby neurodevelopmental conditions such as autism, and sibling health outcomes such as mental health conditions were collectively the most commonly explored [25, 45]. All studies captured sibling data showing some degree of increased risk or higher prevalence of the assessed outcomes among siblings of children and young adults with, compared to those without neurodevelopmental conditions [110]. The poorer outcomes observed for siblings at the population level supports the use of data linkage as a research tool to explore and report health disparities across a diverse range of outcomes. Most studies concluded the shared causal or risk factors prompt the need for further studies [67, 111] to assess genetic and environmental associations in the same study design. Some extended this to recommend preventive and clinical interventions be explored, and early identification and assessment for siblings [65, 66, 79, 103, 107, 112, 113]. These recommendations indicate a real need to increase the focus on sibling data across psychosocial, educational, financial, environmental and other domains.

Limitations for sibling research

It was not an objective of this scoping review to evaluate the findings of the included papers, or to report on data linkage quality [114]. It is acknowledged that poor data quality and linkage error are potential limitations when linking data and may lead to biased results [46]. However, all studies included in this review utilised highly resourced databases and data linkage methods widely considered to be of high standard [81, 82, 115–118]. Despite this we can acknowledge some gaps and inconsistencies present in the reporting of data and methodology in its application to the field of sibling research.

One third of included papers did not contain sufficient detail to describe population characteristics and methodology across studies. This included data relating to population sizes, sibling selection, follow up periods, ages and birth years, age at sibling health outcome, and timeframes of data collection from the various registries. Most papers were published in health discipline journals rather than epidemiological journals that may help to explain some of the inconsistencies and omissions in methodological reporting across the included papers. Improving the reporting of data presentation would allow replication and extension of methodologies in the future, increase validity, and extend the implication of findings, leading to more relevant recommendations for sibling advocacy and supports [84].

In the majority of papers, sibling data were included as a comparison to the index cases and/or controls [119] rather than the primary group of interest. For example, children and young adults with neurodevelopmental conditions were compared with those without these conditions, and with their siblings. Sibling data captured from these comparisons allows general observations on health outcomes, and can help account for unmeasured genetic or shared environmental confounding. However, studies adopting a sibling-focused design can allow assessments of causal inference, and enable perspectives on undiagnosed traits, shared characteristics or diversity that may be present among other family members, improving the context applied to the data and the interpretation of sibling outcomes.

Future sibling research

With the increases in attention given to sibling research over time, and the readiness of data linkage to focus on specific population subgroups, it is expected that increasingly more data linkage studies will capture enhanced sibling data in the future, improving the depth and context of sibling research. In areas where population-based sibling data are available, an obligation exists to broaden the analysis of diagnostic groups and enhance study designs so that siblings are better represented across the full spectrum of disability. A coordinated approach internationally is also possible, to encourage replicability of study design and expansion to similar variables in different locations, increasing validity of findings, and considering rare diagnoses.

Conclusions

This scoping review demonstrated the application of data linkage as an effective method to capture data for siblings of children and young adults with neurodevelopmental conditions at a population level. While a narrow inclusion of geographical areas was represented, increasing data capabilities and more vigilant reporting in the future will help improve the amount and visibility of research conducted with ongoing benefits for addressing the wellbeing of siblings.

Conflicts of interest

The authors report no conflicts of interest in relation to this review.

Ethics statement

Ethical approval for this scoping review was not required.

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Data availability statement

There are no datasets provided in this scoping review, results were collated from selected sources of evidence and presented in summary form and/or in Supplementary Material. Details for each of the sources are available in the references.

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Supplementary Material 1: Scoping review search terms

Search terms used in the databases Ovid (PsycINFO MEDLINE EMBASE); CINAHL Plus (EBSCOhost); SCOPUS (Elsevier); Web of Science (Clarivate) to identify relevant papers

1 Data linkage terms

linked data OR linkage OR medical record* OR administrative data OR routinely collected OR database* OR data base OR data set OR dataset* OR data-set OR data collection* OR register* OR registr* OR statutory OR population data* OR population based OR population-based OR population level OR population-level OR population sample OR national regist* OR nation-wide OR nationwide OR national survey* OR birth cohort* OR prospective cohort

2 Neurodevelopmental conditions terms

neurodevelopment* OR developmental disabilit* OR development* disorder OR development* delay OR intellectual disabilit* OR intellectually disabled OR mental retard* OR mentally retard* OR mental handicap* OR mentally handicapped OR mental disabilit* OR mentally disabled OR learning disorder* OR learning disabilit* OR autis* OR ASD OR Asperger* OR cerebral palsy OR Down* syndrome OR trisomy 21 OR CDKL5 OR Rett syndrome OR Williams syndrome OR Angelman syndrome OR Prader-Willi syndrome OR Cornelia de Lange syndrome OR Phelan#McDermid syndrome OR velocardiofacial syndrome OR 22q13* OR DiGeorge syndrome OR Fragile X OR f#etal alcohol spectrum disorder OR FASD OR attention deficit OR ADHD

3 Sibling terms

sibling* OR brother* OR sister* OR twin* OR family member* OR first-degree OR familial coaggregation OR kin

4 Health outcomes terms

morbidit* OR hospital* OR emergency OR accident* OR ambulance OR admission* OR diagnos* OR DSM* OR ICD* OR health OR risk of OR cancer* OR disease* OR disorder* OR condition* OR chronic illness* OR mortality OR death* OR suicid* OR self harm OR self-harm OR psychiatr* OR psychological OR mental illness* OR anxi* OR depress* OR PTSD OR oppositional OR ODD OR obsessive* OR OCD OR schizophren* OR bipolar OR anorex* OR bulimi*

Running searches 1,2,3 & 4; .ab,ti. (abstract and title search); limiting to years 2000-current (October 2024), peer reviewed.

Supplementary Material 2: Data extraction template

Evidence source characteristics

Authorship
Publication year
Geographic location
Paper aim/focus in relation to siblings

Results extracted from source of evidence

Neurodevelopmental condition of index children
Sibling outcome
Birth year
Age groups
Follow up time
Number and type of registries used
Simplified datasets
Study design
Population size
Paper findings in relation to siblings

Supplementary Material 3: Data extraction table

Authorship Publication year Geographic location	Paper aim/focus (in relation to siblings)	Neuro-developmental condition (of index children)	Sibling outcome	Birth year	Age groups[1] (years represented) *estimated	Follow up time (max years) *estimated	Number and type of registries[2]	Simplified datasets	Study design	Population[3] size	Paper findings (in relation to siblings)
[1] Ahlberg (2022) Sweden https://doi.org/10.1111/jcpp.13538	Risk of obesity among siblings of individuals with autism spectrum disorder (ASD), with/without intellectual disability (ID), and siblings of individuals without ASD.	ASD [+-ID]	Obesity	1973-2006	0-33*	<33*	9: MBR [1973-2006]; TPR; CDR; MGR [>1961]; NPR [1987-2006]; PDR [>2005]; Census [1970-1984]; RAMS [1985-1989]; LISA [1990-2006].	Births, Census, Deaths, Family connections, Hospital, Insurance, Labour, Medication, Total population.	Whole population.	T: 3,141,696 C: 35,461 F: 3,514,560 M: 779,948 P: 735,112	Siblings of individuals with ASD have an increased risk of obesity compared with siblings of individuals without ASD. Greater risk for siblings among ASD -ID subgroup.
[2] Butwicka (2017) Sweden https://doi.org/10.1007/s10803-016-2914-2	Patterns of substance use-related problems among unaffected siblings of individuals with ASD, with/without ID, with/without attention deficit hyperactivity disorder (ADHD).	ASD [+-ID] [+-ADHD]	Substance use related problem	1973-2009	C: 0-36* S: 16, 10-22 (med, IQR)	<36*	11: NPR [>1973]; Pastill; HAB; PDR [>2005]; CDR; NCR; Register of education; Census [1960-1990]; LISA; TPR; MGR.	Census, Crime, Deaths, Education, Family connections, Habilitation, Hospital, Labour, Medication, Psychiatric, Total population.	Matched 1:50 Sex, birth year, country of birth.	C: 26,986 Co: 1,349,300 F: 30,456 H: 15,946	Siblings of individuals with ASD had weakly but significantly increased risk for any substance-related problem compared to controls. With increased risk in the ASD +ADHD & +ID subgroups.
[3] Chang (2019) Taiwan https://doi.org/10.1159/000500831	Risk of developing atopic diseases among unaffected siblings of individuals with ADHD.	ADHD	Atopic disease	1980-2000	C: 14 (4) Co: 15 (6) S: 15 (6) (mean, SD)	<15*	3: NHIRD; Demographic details; Claim information; Recorded family kinships.	Births, Census, Family connections, Hospital, Insurance, Medication, Total population.	Matched 1:4 Age, birth time, residence.	C: 15,122 Co: 80,680 F: 20,170	Siblings of individuals with ADHD had a higher frequency of asthma, atopic dermatitis, allergic rhinitis, and allergic conjunctivitis than the controls.
[4] Chen, M. H. (2019) Taiwan https://doi.org/10.4088/jcp.18m12371	Familial coaggregation of ADHD with other major psychiatric disorders specifically schizophrenia, bipolar, major depressive and ASD.	ADHD	Major psychiatric disorder	Not stated	Not stated	Not stated	3: NHIRD; Demographic details; Claim information; Recorded family kinships.	Births, Census, Family connections, Hospital, Insurance, Medication, Total population.	Matched 1:4 Age, sex, familial relationship.	T: 23,258,175 Co: 1,605,204 S: 174,460	Siblings of individuals with ADHD had a higher relative risk of psychiatric disorder (schizophrenia, bipolar disorder, major depressive disorder, and ASD) than controls.

Continued

Supplementary Material 3: Continued

Authorship Publication year Geographic location	Paper aim/focus (in relation to siblings)	Neuro-developmental condition (of index children)	Sibling outcome	Birth year	Age groups[1] (years represented) *estimated	Follow up time (max years) *estimated	Number and type of registries[2]	Simplified datasets	Study design	Population[3] size	Paper findings (in relation to siblings)
[5] Chen, Q. (2019) Sweden https://doi.org/10.1017/S0033291718002532	Association and familial aggregation of ADHD and clinical obesity in adolescence.	ADHD	Obesity	1973-2000	13-40 C: 22 (7) Co/S: 26 (7) (mean, SD)	<40*	6: MBR [1973-2013]; NPR [1973-2013]; TPR [1932-2013]; LISA; MGR [1932-2013]; PDR [2005-2013].	Births, Family connections, Hospital, Labour, Medication, Total population.	Whole population.	T: 2,538,127 C: 80,009 F: 664,721 M: 68,347 P: 69,350	Siblings of individuals with ADHD showed excess risk for clinical obesity compared to siblings of individuals without ADHD.
[6] Christensen (2016) Denmark https://doi.org/10.1111/epi.13595	Risk of ASD and epilepsy among younger siblings of individuals with ASD and epilepsy.	ASD [+-ID]	Epilepsy	1980-2006	6-32*	<32*	4: Danish medical birth registry; Danish civil registration system; Danish psychiatric central research register; Danish hospital register.	Births, Family connections, Hospital, Psychiatric.	Whole population.	T: 1,663,302	Siblings of individuals with ASD had an increased risk of epilepsy.
[7] Dai (2019) Taiwan https://doi.org/10.1007/s10803-019-04184-w	Risk of developing atopic diseases, including atopic dermatitis, allergic rhinitis, allergic conjunctivitis, and asthma, among the siblings of individuals with ASD.	ASD	Atopic disease	1980-2010	Co/S: 12 (4) (mean, SD)	<15*	3: NHIRD; Demographic details; Claim information; Recorded family kinships.	Births, Census, Family connections, Hospital, Insurance, Medication, Total population.	Matched 1:4 Age, sex, residence.	Co: 11,048S: 2,762	Siblings of individuals with ASD had higher cumulative incidence of asthma, atopic dermatitis, allergic rhinitis, and allergic conjunctivitis than the control group.
[8] Faraone (2017) Sweden https://doi.org/10.1016/j.jaac.2016.11.011	Risk for ADHD in siblings of individuals with ID.	ID [ID severity]	ADHD	1987-2006	0-19*	<19*	6: MBR [1987-2006]; NPR; TPR; MGR; CDR; PDR.	Births, Deaths, Family connections, Hospital, Medication, Total population.	Whole population.	T: 1,899,654 C: 16,158F: 914,848M: 136,962P: 134,502Mt: 4,180Dt: 12,655	Siblings of individuals with ID had an increased risk of ADHD, as compared to siblings of individuals without ID. Greatest risk for siblings seen among the mild ID group.
[9] Ghirardi (2018) Sweden https://doi.org/10.1038/mp.2017.17	Coaggregation of ASD and ADHD in families	ASD [+-ID]	ADHD	1987-2006	Not stated	Not stated	6: MBR [1987-2006]; NPR; TPR; MGR; CDR; PDR.	Births, Deaths, Family connections, Hospital, Medication, Total population.	Whole population.	T: 1,899,654C: 28,468F: 914,848M: 136,962P: 134,502 Mt: 4,180Dt: 12,655	Siblings of individuals with ASD were at increased risk of ADHD than siblings of individuals without ASD. Greatest risk for siblings in the ASD -ID subgroup.

Continued

Supplementary Material 3: Continued

Authorship Publication year Geographic location	Paper aim/focus (in relation to siblings)	Neuro-developmental condition (of index children)	Sibling outcome	Birth year	Age groups[1] (years represented) *estimated	Follow up time (max years) *estimated	Number and type of registries[2]	Simplified datasets	Study design	Population[3] size	Paper findings (in relation to siblings)
[10] Ghirardi (2021) Sweden https://doi.org/10.1111/jcpp.13508	Familial and genetic associations between ASD and other neurodevelopmental and psychiatric disorders.	ASD	Neurodevelopmental disorder, Psychiatric disorder	1985-2009	Not stated	Not stated	2: NPR; TPR.	Hospital, Total population.	Whole population.	T: 2,398,608 C: 33,014	Neurodevelopmental and psychiatric disorders were more common among siblings of individuals with ASD than among siblings of individuals without ASD.
[11] Hegvik (2022) Sweden https://doi.org/10.1093/ije/dyab151	Familial co-aggregation between ADHD and autoimmune diseases.	ADHD	Auto-immune disease	1960/1980-2010	Not stated	Not stated	5: TPR [1960-2010]; CDR; MGR [>1931]; NPR [>1964]; PDR [2005-2013].	Deaths, Family connections, Hospital, Medication, Total population.	Whole population.	T: 5,178,225C: 118,927F: 4,289,186	ADHD was associated with an increased odds of any autoimmune disorders in siblings.
[12] Hirvikoski (2020) Sweden https://doi.org/10.1017/s0033291719001405	Shared familial risk factors for the association between ASD and suicidal behaviour.	ASD [+-ID] [+-ADHD]	Suicide attempt	Not stated	Not stated	Not stated	8: NPR [>1973]; CDR [>1952]; PDR [>2005]; MGR [>1961]; TPR; Census [1970-1984]; RAMS [1985-1989]; LISA [1990-2013].	Census, Deaths, Family connections, Hospital, Insurance, Labour, Medication, Total population.	Matched1:5Sex, year of birth, residence.	C: 54,168Co: 270,840F: 65,994M: 15,915 P: 17,736	The risk of suicide attempts was significantly increased in siblings of individuals with ASD compared to siblings of matched controls. The risk of death by suicide was increased in siblings of individuals with ASD as compared to siblings of the control participants.
[13] Jokiranta-Olkoniemi (2019) Finland https://doi.org/10.1017/s0033291718000521	Psychiatric and neurodevelopmental disorders among siblings of individuals diagnosed with ADHD.	ADHD	Psychiatric disorder, Neurodevelopmental disorder	C: 1991-2005 S: 1981-2007	C: 6-20* S: 6-32*	<32*	3: FCPR; FHDR [>1969]; FMBR [>1987].	Births, Hospital, Total population.	Matched1:4Sex, date and place of birth.	T: 900,603C: 7,369Co: 23,181F: 12,565	Siblings of individuals with ADHD had increased risk for all psychiatric and neurodevelopmental conditions than controls, except eating disorders.
[14] Jokiranta-Olkoniemi (2016) Finland https://doi.org/10.1001/jamapsychiatry.2016.0495	Risk for psychiatric and neuro-developmental disorders among siblings of individuals with ASD.	ASD [+-ID]	Psychiatric disorder, Neurodevelopmental disorder	C: 1987-2005S: 1977-2005	C: 2-20*S: 4-32*	<32*	3: FCPR; FHDR [>1969]; FMBR [>1987].	Births, Hospital, Total population.	Matched 1:4 Sex, date and place of birth.	C: 3,578 Co: 11,775 F: 6,022	The rates of all investigated psychiatric and neurodevelopmental disorders (except alcohol and drug addiction or abuse) were elevated among the siblings of individuals with ASD compared with the siblings of controls. For ASD +-ID greatest risk differences seen for schizophrenia, learning and conduct disorders.

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Supplementary Material 3: Continued

Authorship Publication year Geographic location	Paper aim/focus (in relation to siblings)	Neuro-developmental condition (of index children)	Sibling outcome	Birth year	Age groups[1] (years represented) *estimated	Follow up time (max years) *estimated	Number and type of registries[2]	Simplified datasets	Study design	Population[3] size	Paper findings (in relation to siblings)
[15] Kuja-Halkola (2021) Sweden https://doi.org/10.1038/s41380-018-0248-5	Co-occurrence and familial co-aggregation between clinically diagnosed ADHD and borderline personality disorder (BPD).	ADHD	BPD	1979-2001	12-34*	<34*	7: MBR [1979-2001]; CDR; TPR; MGR; Twin register; NPR [2001-2013]; PDR [2005-2014].	Births, Deaths, Family connections, Hospital, Medication, Total population, Twins.	Whole population.	T: 2,113,902 C: 82,593 F: 2,211,396 M: 332,486 P: 331,080	Sibling of individuals with ADHD had increased odds of having BPD.
[16] Larsson (2013) Sweden https://doi.org/10.1192/bjp.bp.112.120808	Occurrence of bipolar disorder and schizophrenia in relatives of individuals with ADHD.	ADHD	Bipolar disorder, Schizophrenia	C: 1932-2009	Not stated	<77 *	6: NPR [>1973]; PDR [>2005]; TPR [<2009]; CDR [1952-2009]; MGR; Twin register.	Deaths, Family connections, Hospital, Medication, Total population, Twins.	Matched 1:10 Sex, birth year.	C: 61,187	Siblings of individuals with ADHD were at increased risk of both bipolar disorder and schizophrenia.
[17] Lin (2022) Taiwan https://doi.org/10.1007/s00787-021-01784-9	Developmental and mental disorders among unaffected siblings of individuals with ASD.	ASD	Developmental disorder, Mental disorder	Co/S: 1980-2010	Co/S: 1-31* Co/S: 14 (7) (mean, SD)	<15	3: NHIRD; Demographic details; Claim information; Recorded family kinships.	Births, Census, Family connections, Hospital, Insurance, Medication, Total population.	Matched 1:10 Age, sex, birth year, family structure.	Co: 13,040; S: 1,304	Siblings of individuals with ASD had a higher prevalence of any developmental disorder and any mental disorder (except for bipolar) compared with the controls.
[18] Liu (2022) Sweden https://doi.org/10.1016/j.annonc.2022.04.006	Sibling comparison to address familial confounding between ASD and cancer.	ASD [+-ID]	Cancer	1973-2013	3-30	<30	5: MBR [1973-2013]; NPR [1973-2016]; MGR [1932-2016]; Cancer register [1958-2016]; LISA [1990-2016].	Births, Cancer, Family connections, Hospital, Insurance.	Whole population.	T: 2,354,594 C: 40,334 Co: 2,278,100 F: 36,160	We found a statistically significant increased risk of any cancer among siblings of individuals with ASD compared with controls.
[19] Liu (2021) Sweden https://doi.org/10.1371/journal.pmed.1003840	Association between ID and risk of cancer, using a sibling comparison to adjust for potential familial confounding.	ID [ID severity]	Cancer	1974-2013	3-43*	<43	5: MBR [1973-2013]; MGR [1932-2016]; NPR [1987-2016]; Cancer register [1958-2016]; LISA [<2016].	Births, Cancer, Family connections, Hospital, Insurance.	Whole population.	T: 3,531,305 C: 27,956 F: 29,641	Siblings of individuals with ID, compared with the reference group, had a higher risk of subsequent cancer.

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Supplementary Material 3: Continued

Authorship Publication year Geographic location	Paper aim/focus (in relation to siblings)	Neuro-developmental condition (of index children)	Sibling outcome	Birth year	Age groups[1] (years represented) *estimated	Follow up time (max years) *estimated	Number and type of registries[2]	Simplified datasets	Study design	Population[3] size	Paper findings (in relation to siblings)
[20] Ljung (2014) Sweden https://doi.org/10.1001/jamapsychiatry.2014.363	Risk of suicide in individuals with ADHD and the familial risk for siblings.	ADHD	Suicide attempt, Completed suicide	Not stated	Not stated	Not stated	5: NPR [1987-2009]; PDR [2005-2009]; MGR [1932-2009]; TPR [1969-2009]; CDR [1952-2009].	Deaths, Family connections, Hospital, Medication, Total population.	Matched 1:5 Sex, birth year.	C: 51,707 Co: 258,535 F: 58,589 M: 20,246 P 21,631	Siblings of individuals with ADHD were more likely to attempt suicide and had an increased risk of completed suicide compared with siblings of control participants.
[21] Marquis (2019) Canada https://doi.org/10.1016/j.ssmph.2019.100441	Differences in the mental health of siblings of individuals with a developmental disability and siblings with no developmental disability in the family.	Developmental disability	Depression, Mental health problem	S: 1990-1995 2000-2005	S: 0-19	<24	3: Population data B.C. Central consolidation file: demographics [1990-2014]; Medical services plan: Fee for service care [1990-2014]; Hospital separation file: hospitalisations [1990-2014].	Hospital, Physician care, Total population.	Whole population.	Co: 880,972 S:18,295	Siblings of individuals with a developmental disability had greater odds of a diagnosis of depression or of another mental health problem (excluding depression) compared to siblings of individuals without a developmental disability.
[22] Nimmo-Smith (2020) Sweden https://doi.org/10.1007/s10803-019-04234-3	Risk for diagnosis of anxiety disorders across ASD cases; their full siblings; their half-siblings; and a reference population.	ASD [+-ID]	Anxiety disorder	Not stated	18-27	Not stated	4: SYC [2001-2011]; NPR [>1973]; Stockholm adult psychiatric outpatient register [>1997]; Pastill [>1999].	Hospital, Psychiatric (adolescent/adult), Total population.	Whole population.	T: 221,694 C: 4,049	Comparing the ASD cases with their non-autistic siblings, risk of anxiety disorder was highest amongst the ASD cases than their siblings, and risks were raised in siblings compared with the general population. Sibling risks were highest for subgroup ASD (-ID).
[23] Pahlsson-Notini (2024) Sweden https://doi.org/10.002/jcv2.12225	Substance use-related problems among siblings of individuals with mild ID.	Mild ID	Substance use-related problem, Anxiety disorder, Major depressive disorder, Bipolar disorder, Psychotic disorder, ADHD, ASD	1973-2003	10-40*	<40*	11: NPR [1973-2013]; Pastill [2001-2013]; HAB [1997-2013]; HURPID [2001-2013]; CDR [1973-2013]; LISA [1990-2013]; MGR [1973-2013]; NCR [1973-2013]; PDR [2005-2013]; MBR [1973-2003]; TPR [1973-2013].	Births, Crime, Deaths, Education, Family connections, Habilitation, Hospital, Insurance, Medication, Psychiatric (adolescent), Total population.	Matched 1:50 Age, sex, birth region.	T: 2,980,565 C: 18,307 Co: 915,350 C: 12,005 F: 18,996	Siblings of individuals with mild ID had an increased risk for substance use-related problems.

Continued

Supplementary Material 3: Continued

Authorship Publication year Geographic location	Paper aim/focus (in relation to siblings)	Neuro-developmental condition (of index children)	Sibling outcome	Birth year	Age groups[1] (years represented) *estimated	Follow up time (max years) *estimated	Number and type of registries[2]	Simplified datasets	Study design	Population[3] size	Paper findings (in relation to siblings)
[24] Rai (2018) Sweden https://doi.org/10.1001/jamanetworkopen.2018.1465	Risk of individuals with ASD to be diagnosed with depression compared to the general population and their non-autistic siblings.	ASD [+-ID]	Depression	Not stated	18-27	Not stated	5: SYC [2001-2011]; NPR [>1973]; Stockholm adult psychiatric outpatient register [>1997]; Pastill [>1999]; MGR.	Family connections, Hospital, Psychiatric (adolescent/adult), Total population.	Whole population.	T: 223,842 C: 4,073	Siblings of individuals with ASD had a higher risk of depression compared with population controls. Sibling risks were highest for subgroup ASD (-ID).
[25] Selten (2015) Sweden https://doi.org/10.1001/jamapsychiatry.2014.3059	Risks for non-affective psychotic disorder (NAPD), and bipolar disorder in individuals with ASD compared to individuals without ASD and their non-affected siblings.	ASD [+-ID]	NAPD, Bipolar disorder	1984>	C/Co: 15 (6) (mean, SD)	Not stated	3: SYC [2001-2011]; NPR [>1973]; Stockholm adult psychiatric outpatient register [>1997].	Hospital, Psychiatric, Total population.	Matched 1:10 Age, sex.	T: 689,333 C: 19,788Co: 197,880 F: 23,905	Siblings of individuals with ASD showed greater risks for NAPD and bipolar disorder than controls. Sibling risks were similar for ASD+-ID subgroups.
[26] Stark (2022) Sweden https://doi.org/10.1111/acps.13479	Family level confounding and the link between ASD and self-harm.	ASD [+-ID]	Self-harm	Not stated	10-27 C: 17 (4) Co: 18 (5) (mean, SD)	<17*	5: SYC [2001-2011]; NPR [>1973]; Stockholm adult psychiatric outpatient register [>1997]; Pastill [>1999]; MGR.	Family connections, Hospital, Psychiatric (adolescent/adult), Total population.	Whole population.	T: 410,732 C: 9,070	Siblings of individuals with ASD had a higher risk of self-harm as compared with population controls. Sibling risks were highest for subgroup ASD (-ID).
[27] Sundquist (2015) Sweden https://doi.org/10.1017/S0033291714001986	Causal relationship between ADHD and drug use disorder by using a co-relative design.	ADHD	Drug use disorder	1991-1995	6-20*	<20*	9: TPR; MGR; Hospital discharge register [1964-2010]; PDR [2005-2010]; Outpatient care register [2001-2010]; NCR [1973-2011]; Suspicion register [1998-2011]; Mortality register; LISA.	Crime, Deaths, Family connections, Hospital, Insurance, Medication, Outpatient, Suspicion, Total population.	Whole population.	T: 551,164 F: 3,410 H: 610	Siblings of individuals with ADHD had an increased risk for future drug use disorders.

Continued

Supplementary Material 3: Continued

Authorship Publication year Geographic location	Paper aim/focus (in relation to siblings)	Neuro-developmental condition (of index children)	Sibling outcome	Birth year	Age groups[1] (years represented) *estimated	Follow up time (max years) *estimated	Number and type of registries[2]	Simplified datasets	Study design	Population[3] size	Paper findings (in relation to siblings)
[28] Taylor (2022) Sweden https://doi.org/10.1111/jcpp.13473	Links between ASD and difficulties initiating and maintaining sleep within the same families.	ASD	Insomnia	1973-2013	1-40*	<40*	6: MBR [1973-2013]; MGR; CATSS [>1992]; NPR [1973-2013]; TPR; PDR [2005-2013].	Births, Family connections, Hospital, Medication, Total population, Twins.	Matched 1:50 Sex, year and place of birth.	C: 50,097 F: 55,967 M: 15,027 P: 16,642 Mt: 60 Dt: 340	Siblings of individuals with ASD were more likely to have difficulties initiating and maintaining sleep than controls.
[29] Tollanes (2016) Norway https://doi.org/10.1542/peds.2016-0269	Underlying causes of cerebral palsy (CP) and other neurodevelopmental disorders in siblings of individuals with CP.	CP	Neurodevelopmental disorder	1967-2006	5-44*	<44*	3: Medical birth registry of Norway [1967-2006]; Norwegian national insurance scheme [<2007]; Norwegian patient registry [2008-2011].	Births, Hospital, Insurance.	Whole population.	C: 5,707 F: 1,381,347 Tw: 26,485	Siblings of individuals with CP are at increased risk of other neurodevelopmental disorders.
[30] Wang (2022) Taiwan https://doi.org/10.1017/s0033291720003207	Genetic influence on ASD and major psychiatric disorders by examining all first-degree relative types.	ASD [+-ID]	Psychiatric disorder	Not stated	Not stated	Not stated	3: NHIRD; Demographic details; Claim information; Recorded family kinships.	Births, Census, Family connections, Hospital, Insurance, Medication, Total population.	Matched 1:4 Age, sex, familial relationship.	T: 23,258,175 C: 26,667	Siblings of individuals with ASD had a higher risk for all major psychiatric disorders when compared to controls.
[31] Wei (2019) Taiwan https://doi.org/10.1016/j.jad.2018.11.057	Mental and physical health risks among the unaffected siblings of individuals with ADHD.	ADHD	Mental health risk, Physical health risk	1980-2000	C 15 (4) Co: 17 (5) S: 17 (4) (mean, SD)	<15	3: NHIRD; Demographic details; Claim information; Recorded family kinships.	Births, Census, Family connections, Hospital, Insurance, Medication, Total population.	Matched 1:4 Age, sex, birth time.	C: 5,253 Co: 20,512 S: 5,128	Siblings of individuals with ADHD were more likely than controls to have mental and physical health risks (including unipolar depression, bipolar disorder, and traumatic brain injury).

[1]The full list of population groups is provided at the end of the table.
[2]The full list of registries is provided at the end of the table.
[3]The full list of population groups is provided at the end of the table.

Registries: Sweden: Medical Birth Register (MBR); Total Population Register (TPR); Cause of Death Register (CDR); Multi Generation Register (MGR); National Patient Register (NPR); Cancer register; Prescribed Drug Register (PDR); Clinical database for child and adolescent psychiatry; Habilitation register (HAB); Outpatient care register; National Crime Register (NCR); Suspicion register; Mortality register; Register of education; Census (population and housing census); Register-based labor market statistics (RAMS); Longitudinal integration database for health insurance and Labour market studies (LISA); Stockholm Youth Cohort (SYC); Stockholm adult psychiatric outpatient register; Stockholm child and adolescent mental health register (Pastill); Halmstad University Register on Pupils with Intellectual Disability (HURPID). Taiwan: National Health Insurance Research Database (NHIRD); Demographic details (date of birth, sex, monthly premium, and residential location); Claim information (outpatient and inpatient care, medical diagnoses, prescriptions, and operations); Recorded family kinships. Finland: Finnish Central Population Register (FCPR); Finnish Hospital Discharge Register (FHDR); Finnish Medical Birth Register (FMBR). Denmark: Danish medical birth registry; Danish civil registration system; Danish psychiatric central research register; Danish hospital register. Norway: Medical Birth Registry of Norway (MBRN); Norwegian national insurance scheme; Norwegian patient registry. Canada: Population data B.C (PopData); Central consolidation file; Medical Services Plan (MSP); Hospital separation file.

Populations: Total eligible (T); Cases/exposure (C); Controls (Co); Siblings (S); Full siblings (F); Half siblings (H); Maternal siblings (M); Paternal siblings (P); Twins (T); Monozygotic twins (Mt); Dizygotic twins (Dt).

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