



Review Article

Psychiatric morbidity in bladder exstrophy-epispadias complex: A systematic review with a population-based case-control study

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Summary

Introduction

Bladder exstrophy and epispadias complex is a rare congenital anomaly with significant medical and psychosocial implications. We employed a dual approach to evaluate the prevalence and risk factors of psychiatric morbidity in bladder exstrophy and epispadias patients, by combining a systematic review with a retrospective national registry study.

Objective

To evaluate the prevalence and risk factors of psychiatric morbidity in bladder exstrophy and epispadias complex.

Methods

We conducted a systematic literature review following Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines, including studies on psychiatric disorders or symptoms and quality of life in bladder exstrophy and epispadias patients of all ages. Article quality was assessed using the Newcastle–Ottawa Scale. Prevalence data for psychiatric conditions and scores from psychiatric and quality-of-life questionnaires were extracted.

Additionally, all bladder exstrophy and epispadias patients born in Finland 2001–2006 were

identified from national registries. A matched and randomized control group without congenital malformations was selected from the same population. We evaluated the prevalence and risk factors for psychiatric diagnoses in this cohort.

Results

Of the 3850 retrieved results, 30 studies with 1179 participants were included. The overall prevalence of psychiatric morbidity was 31 %, [95 % CI 17 %–47 %]. Psychiatric morbidity was highest in adolescents, while morbidity in adults was comparable to the general population.

In the Finnish cohort, 80 % (n = 16/20) of bladder exstrophy and epispadias patients had a psychiatric diagnosis compared to 26 % (n = 21/80) of the controls (OR 11.2, [95 % CI 3.37–37.4], p < 0.001). The severity of the anomaly, number of surgeries, maternal unemployment, or maternal psychiatric diagnosis were not significantly associated with increased psychiatric morbidity.

Conclusions

Bladder exstrophy and epispadias is associated with an elevated risk of psychiatric morbidity. Our dual approach highlights the need for systematic mental health assessment and support in this population.

Introduction

Bladder exstrophy and epispadias complex (BEEC) is a rare congenital anomaly, with varying severity ranging from mild epispadias to complete cloacal exstrophy. Classic bladder exstrophy is characterized by the exposure of the inner surface of the urethra and posterior bladder wall through the abdomen. This occurs when the abdominal wall and underlying structures, including the ventral wall of the bladder and pubic symphysis, fail to fuse in the early stages of development [1]. Epispadias is

a less severe form of this anomaly, where only the urethra remains dorsally unfused. Cloacal exstrophy represents the most severe end of the spectrum and involves both the bladder and bowel.

The severity of BEEC anomalies can lead to significant medical stress during childhood and adolescence. The stress of living with the condition is compounded by the treatment regimen, which may involve multiple surgical procedures aimed at achieving urinary continence and satisfactory genital appearance [1]. A substantial part of the published literature

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on the long-term outcomes of BEEC has focused on surgical results, continence, sexual function, and fertility. However, these studies often overlook mental health outcomes [2–4]. In addition, the existing literature on the long-term mental health of these patients is incongruent. While some studies have reported normal psychosocial functioning [5–8], others have identified significantly elevated levels of anxiety and depression in this population [9–12]. Moreover, much of the existing research exploring the mental health aspect of BEEC has focused on general quality of life (QoL), psychosocial aspects, and sexual health without comprehensively assessing psychiatric morbidity [13,14].

We aim to clarify the prevalence and risk factors for psychiatric disorders in BEEC patients through a dual approach. To evaluate the burden of psychiatric morbidity, we combine a systematic review of the current literature with a nationwide, population-based register study in Finland. In the registry study, we assess the prevalence and distribution of psychiatric diagnosis in BEEC patients born between 2001 and 2006, compared to age- and gender-matched randomized controls without congenital malformations, with up to 22 years of follow-up. By integrating these complementary methods, we seek to enhance the understanding of the psychiatric challenges faced by BEEC patients and provide insights to ultimately enable more personalized and improved care.

Methods

Systematic review

Search strategy

The main search phrases were 'bladder exstrophy', 'epispadias' or 'cloacal exstrophy' in combination with either 'mental health', 'mental disorder', 'mental illness', 'psychiatric illness', 'psychiatric symptom', 'behavioral health', 'behavioral disorder', 'behavioral problem', 'behavioral disturbance', 'emotional disorder', 'health-related quality of life', 'psychosocial', 'psychopathology', 'psychosis', 'psychotic', 'neuropsychiatry', 'depression', 'anxiety', 'suicide', 'panic', 'self-harm', 'self-injury', 'ADHD', 'sleep disorder' or 'mood disorder'. All different occurrences of search terms were built into the searches. For comprehensiveness, the search was conducted from inception till 16 May 2024 (date of last search) across multiple databases: PubMed, Cochrane Library, Embase, Scopus, ProQuest, Science Direct, Web of Science, and PsycINFO.

Inclusion and exclusion criteria

We included empirical studies with patients with bladder exstrophy, epispadias, or cloacal exstrophy in conjunction with a psychiatric diagnosis or symptoms indicating a psychiatric disorder without a definitive diagnosis, as is often the case with a pediatric population. To be included, the study had to report the psychiatric diagnoses found or symptoms indicative of psychiatric illness, even if no formal diagnosis was made. Symptoms could be assessed by reviewing medical records, structured interviews, or using a self-made or standardized questionnaire. We also included studies where it was possible to separately assess

a general mental health domain included in a quality-of-life questionnaire. In studies that reported on a wider population of congenital malformations or other chronic conditions, we included the ones where selective data on BEEC patients could be extracted. All age groups, from children to adults, were included in the systematic review due to the scarcity of data on pediatric BEEC patients' mental health. Studies reporting only on psychosocial attributes such as relationship status, educational achievements, or employment were excluded. Articles not available in English were excluded. Only original articles were included.

Study selection

The initial search results were pooled, and duplicates were removed automatically. Titles and abstracts were screened by E.K. Reports meeting the initial criteria were retrieved, and their full texts were independently assessed by E.K. and L.R. against the eligibility criteria. Discrepancies were solved by N.P. Citation searching for the eligible reports' reference list was conducted. No attempt to identify grey literature was made.

Data collection process

The number, age, gender, and bladder exstrophy diagnosis severity of the patients were extracted from each report. Additionally, the characteristics of the reports such as authors, journal, year of publication, study design, and methods used to assess psychiatric problems were collected from the reports. The prevalence of psychiatric diagnoses or clinically relevant psychiatric symptoms was extracted from the reports by E.K. and L.R. to limit errors and bias. Studies that used psychiatric questionnaires, the mean raw scores or t-scores and standard deviations were extracted. If the study reported the control group data or normative data used, those were extracted. If not, normative data from the questionnaire manual or a similar population was used to calculate effect sizes. The same method was used for QoL questionnaire data, but only the mental health domain scores were included.

Quality analysis

To control for bias and to ensure the reliability of results, the methodological quality of the included reports was assessed independently by E.K. and L.R. using the Newcastle-Ottawa Scale [15] for case–control studies and a modified Newcastle–Ottawa scale for cross-sectional studies (Attachment 1). Both scales rated the studies across three domains: selection, comparability, and outcome resulting in a score ranging from 0 to 9 stars. Studies with 7–9 stars were considered good, 4–6 stars fair, and 0–3 stars poor quality.

Statistical analysis

We applied the random effects model to obtain meta-analytic estimates for the prevalence of psychiatric morbidity in BEEC patients, and for summary effect sizes of psychiatric questionnaire scores and QoL in the mental health domain of BEEC patients versus controls [16]. Both the scores of the psychiatric questionnaires and the QoL questionnaire results were transformed into standardized effect sizes (Hedges' *g*) prior to analysis. We performed subgroup analyses of both psychiatric questionnaire scores

by type of psychopathology and prevalence by age and diagnosis group. The analyses were carried out using the MetaXL-package [17].

National register study

Study patients and data collection

We performed a retrospective registry-based cohort study including all children born in Finland between 2001 and 2006 ($n = 341\,632$). The data was collected from Finnish national registries including the National Birth Register, Finnish Care Register for Health Care (CRHC), and Cause of Death Register. The upkeep of these registries is mandated by law and the data is retrospectively collected from all hospitals and health centers in mainland Finland, which ensures the accuracy and coverage of the data. Follow-up data was available until 2022-12-31 resulting in a follow-up of 16–22 years.

This data was pooled by the Social Finnish Health Data Permit Authority Findata. All patients with either or both ICD-10 diagnosis code Q64.0 Epispadias and Q64.1 Bladder exstrophy were identified from pooled registry data [18]. Their sex, other diagnoses, surgical procedures, and maternal psychiatric diagnoses were extracted. Maternal employment status when expecting the child was used as a proxy variable of socioeconomic status, as this was readily available data in the registry and is a well-established indicator of socioeconomic position in health research [19]. Any recorded diagnosis code in the ICD-10-chapter V 'Mental and behavioral disorders' was considered as a psychiatric diagnosis (F00–F99). Due to ICD-10 grading, bladder exstrophy and cloacal exstrophy patients were pooled together. We excluded patients who did not have any surgical repairs associated with BEEC according to the registry. We also excluded patients with epispadias diagnosis that had only a meatoplasty procedure, as this suggests a very minor meatal malformation rather than primary epispadias. Some subjects with BEEC diagnosis were found to have additional genitourinary conditions, such as hypospadias, posterior urethral valve, cloaca, or urethral stricture. The procedures performed on these patients suggested that BEEC was a misdiagnosis early in life and these subjects were excluded from the study. All other children with BEEC diagnosis were included regardless of their comorbidities.

The control group of subjects was selected from the same birth cohort in a 4:1 case-to-control ratio. Subjects with any congenital anomaly were excluded before selection. The control group was matched to the case group by birth date and sex.

Statistical analysis

We applied logistic regressions of psychiatric morbidity of the child upon BEEC diagnosis, both with and without controlling for psychiatric morbidity of the mother and maternal unemployment, in a group of 20 BEEC patients and 80 randomly selected age and sex-matched controls. Differences in psychiatric morbidity between children with epispadias only versus children with bladder or cloacal exstrophy were assessed with Fisher's exact test. Within the BEEC group, we also applied logistic regression to the

number of surgeries to assess its possible association with psychiatric morbidity. The analyses were carried out using SAS for Windows version 9.4 (SAS Institute Inc., Cary, NC, USA). Two-sided p-values below 0.05 were considered statistically significant. Results were expressed with odds ratios (OR) with 95 % confidence intervals (95 % CI).

Ethics

The systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO CRD42024538255) on 2024-07-12. The objectives of the review were to determine whether BEEC patients experience higher rates of psychiatric symptoms or diagnoses compared to the general population. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [20].

For the register study, personal patient information is processed by Findata so that individuals cannot be identified from the data. Therefore, informed consent of the patients or their guardians was not needed. The study was approved by the Finnish Institute for Health and Welfare and Findata (THL/2407/14.02.00/2024). The legal basis for processing personal data is public interest and scientific research (EU General Data Protection Regulation 2016/679 (GDPR), Article 6 (1) (e) and Article 9 (2) (j); Data Protection Act, Sections 4 and 6).

Results

Systematic review

The systematic review identified 3850 articles, 30 of which were eligible and included in the final analysis. These studies involved 1179 participants: 875 (74 %) with bladder exstrophy, 144 (12 %) with primary epispadias, and 121 (10 %) with cloacal exstrophy, while two studies did not disclose BEEC severity. The mean age of participants was 20.4 years, ranging from two to 73 years, and 439 (37 %) were female. Study demographics and quality assessments, summarized in Table 1, classified eight studies as good, 17 as fair, and five as poor. A flowchart of the study selection is presented in Fig. 1.

Quantitative synthesis of systematic review data

The pooled prevalence of psychiatric morbidity in BEEC patients was 31 % [95 % CI 17 %–47 %], Fig. 2. Sufficient data for quantitative analysis were available from 18 studies: five used interviews to assess psychiatric diagnoses, 12 employed one or more (either self-made or validated) questionnaires, and one relied on chart review.

Overall, the 30 studies used 30 different questionnaires, 12 of which targeted psychopathology, and nine focused on quality of life (QoL). Data from 14 psychiatric questionnaires across nine studies were sufficient for analysis, with results grouped by psychopathology. The overall summary effect in psychiatric questionnaire scores was -0.47 [95 % CI -1.08 to 0.14], reflecting slightly worse outcomes for BEEC patients than the general population, though not statistically significant. Heterogeneity was notably high ($I^2 = 97$ %). Behavioral symptoms were the most commonly

Table 1 Study demographics and quality assessment of studies on psychiatric morbidity of patients with bladder exstrophy and epispadias complex.

First author	Year	Study design	Patient population				Sex Female (%)	Age		Quality score				
			Total	BE	PE	CE		Mean (y)	Range (y)	S	C	O	Total	
Feitz	1994	CS	22	22	0	0	11 (50 %)	29	17–55	2	0	1	3	Poor
Diseth [12]	1998	C–C	22	19	3	0	5 (23 %)	14,5	11–20	4	2	1	7	Good
Montagnino [8]	1998	CS	29	20	0	9	19 (66 %)	7,8	3–18	4	2	3	9	Good
Reiner	1999	CS	14	14	0	0	0 (0 %)	16,2	14–19	2	0	2	4	Fair
Stjernqvist	1999	CS	15	15	0	0	8 (53 %)	11,3	3–18	2	1	2	5	Fair
Baker Towell	2003	C–C	8	0	0	8	NA	11,3	5–18	4	2	2	8	Good
Wilson [5]	2004	CS	16	16	0	0	5 (31 %)	19	16–21	1	0	1	2	Poor
Catti	2006	CS	23	22	0	1	23 (100 %)	26,5	19–41	3	0	1	4	Fair
Reiner [11]	2006	CS	20	NA	NA	NA	NA	32	5–22	2	0	1	3	Poor
Mukherjee [6]	2007	CS	9	0	0	9	6 (67 %)	22,11	11–37	2	1	3	6	Fair
Reiner	2008	CS	121	121	0	0	25 (21 %)	NA	5–24	4	0	2	6	Fair
Dodson [10]	2010	CS	55	48	7	0	17 (31 %)	14	11–18	3	0	2	5	Fair
Ebert	2010	CS	17	16	1	0	0 (0 %)	23,4	18,3–33,9	2	0	0	2	Poor
Jochault-Ritz	2010	CS	71	71	0	0	30 (42 %)	16,4	6–42	3	2	2	7	Good
Wittmeyer	2010	CS	25	25	0	0	9 (36 %)	30,5	19,5–49,5	3	0	2	5	Fair
Schaeffer	2012	CS	57	49	8	0	19 (33 %)	14,3	11–18	3	2	2	7	Good
Gupta [9]	2014	CS	21	21	0	0	6 (29 %)	NA	27–37	3	0	1	4	Fair
Hankinson	2014	CS	86	61	25	0	33 (38 %)	7,97	3–16	3	2	3	8	Good
Deans [7]	2015	CS	28	28	0	0	28 (100 %)	32	17–46	3	0	2	5	Fair
Hurrell	2015	CS	80	51	22	7	30 (38 %)	8,41	1–18	4	2	3	9	Good
Taskinen [21]	2015	CS	33	20	13	0	11 (33 %)	27	15–52	3	1	3	7	Good
Amesty	2016	CS	9	0	9	0	9 (100 %)	20,30	5–39	3	0	2	5	Fair
Bujons	2016	CS	19	NA	NA	NA	19 (100 %)	26	18–50	2	0	2	4	Fair
da Cruz	2016	CS	43	43	0	0	14 (33 %)	22,35	15–36	3	1	2	6	Fair
Traceviciute [22]	2018	CS	19	16	3	0	0 (0 %)	26	22–38	2	0	2	4	Fair
Zhu	2020	CS	17	12	4	1	8 (47 %)	36	19–73	1	0	2	3	Poor
Ben Ahmed	2022	CS	15	15	0	0	4 (27 %)	14	5–25	2	0	2	4	Fair
de Jesus	2022	CS	50	48	0	2	26 (52 %)	32,36	19–50	2	2	2	6	Fair
Gittins [23]	2024	CS	172	102	49	21	52 (30 %)	9,9	2–17	2	2	2	6	Fair
Haney	2024	CS	63	0	0	63	22 (35 %)	21,1	14,8–27,7	4	0	0	4	Fair
Total			1179	875	144	121	439 (37 %)	20,4						

CS = cross-sectional; C–C = case–control; BE = bladder exstrophy; PE = primary epispadias; CE = cloacal exstrophy; NA = not available; S = selection; C = comparability; O = outcome; Quality assessment: Good: 7–9 stars, Fair: 4–6 stars, Poor: 0–3 stars.

assessed psychiatric domain, which yielded the poorest summary effect, suggesting that behavioral problems were the most prevalent issue among BEEC patients. General behavioral assessment questionnaires were used, for example Child Behavior Checklist and Behavior Assessment Score for Children. These behavioral symptoms were found to be both internalizing and externalizing in nature, with no single identifiable diagnosis more common than others.

QoL mental health domain results were extracted from 11 studies. The summary effect was -0.29 [95 % CI -0.54 to -0.04], suggesting a minimally worse mental health aspect in BEEC patients' QoL, accompanied by substantial heterogeneity ($I^2 = 86$ %).

Subgroup analyses of systematic review data

To explore the high heterogeneity observed in the results, we performed subgroup analyses to evaluate the influence of age and BEEC severity on the prevalence data.

We categorized study populations into children (<13 years), adolescents (13–22.99 years), and adults (≥ 23 years) based on age range or mean age. One study that did

not disclose the age of the participants was excluded from the subgroup analyses. Fig. 3 presents the age subgroup analyses, which revealed that adolescents had the highest prevalence of psychiatric diagnoses (39 % [95 % CI 2 %–81 %]) compared to children (26 % [95 % CI 8 %–48 %]) and adults (17 % [95 % CI 7 %–31 %]). The most common diagnoses found were anxiety disorder secondary to a medical condition, major depressive disorder and obsessive-compulsive disorder.

Next, we examined BEEC severity as a risk factor. Studies reporting only on bladder exstrophy or cloacal exstrophy were analyzed separately. Out of the studies that reported prevalence, no studies exclusively assessed primary epispadias patients, and only two studies focused solely on cloacal exstrophy. Data could not be extracted separately by diagnosis from the ten studies that included all BEEC severity categories collectively; therefore, those studies were excluded. Only two studies remained in the cloacal exstrophy group and six in the bladder exstrophy group. No significant difference in the prevalence of psychiatric diagnoses was found between these subgroups.

Algorithm for study selection modified from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart

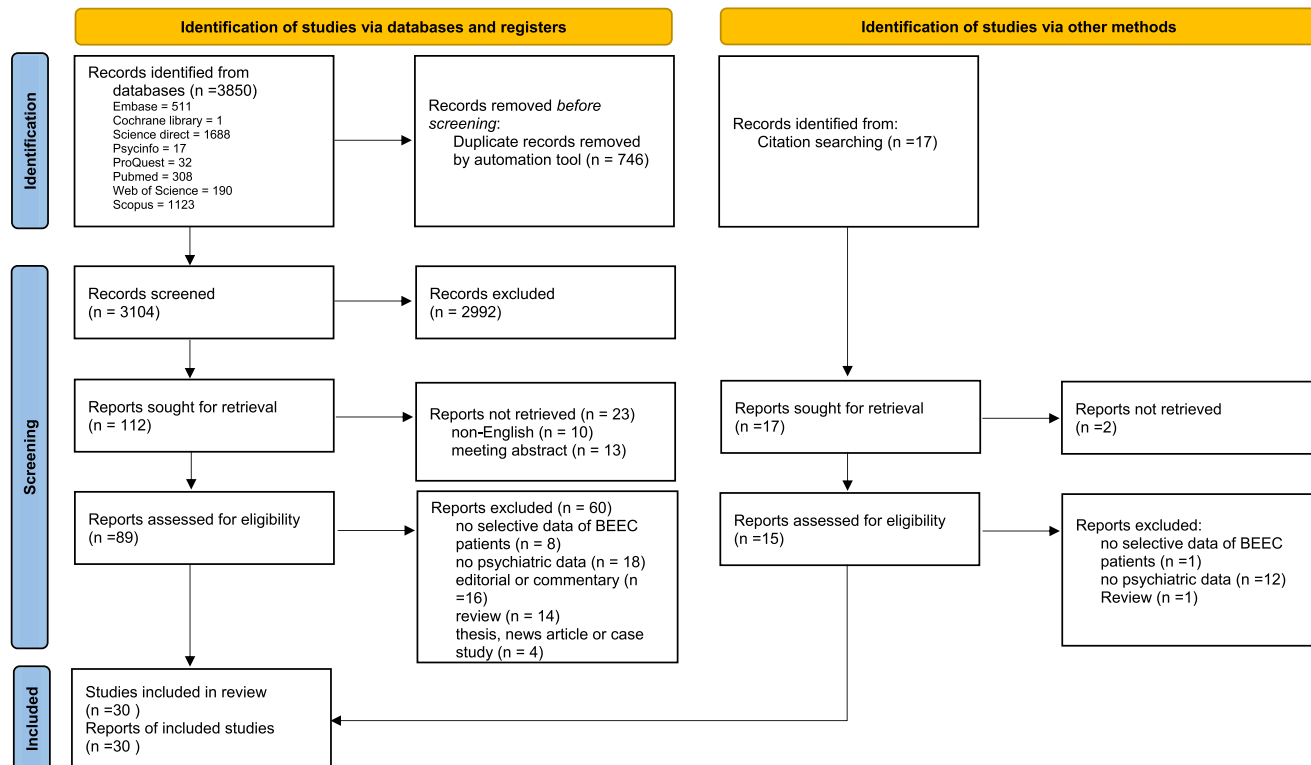


Fig. 1 Study selection flowchart modified from Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines [20]. BEEC = bladder exstrophy and epispadias.

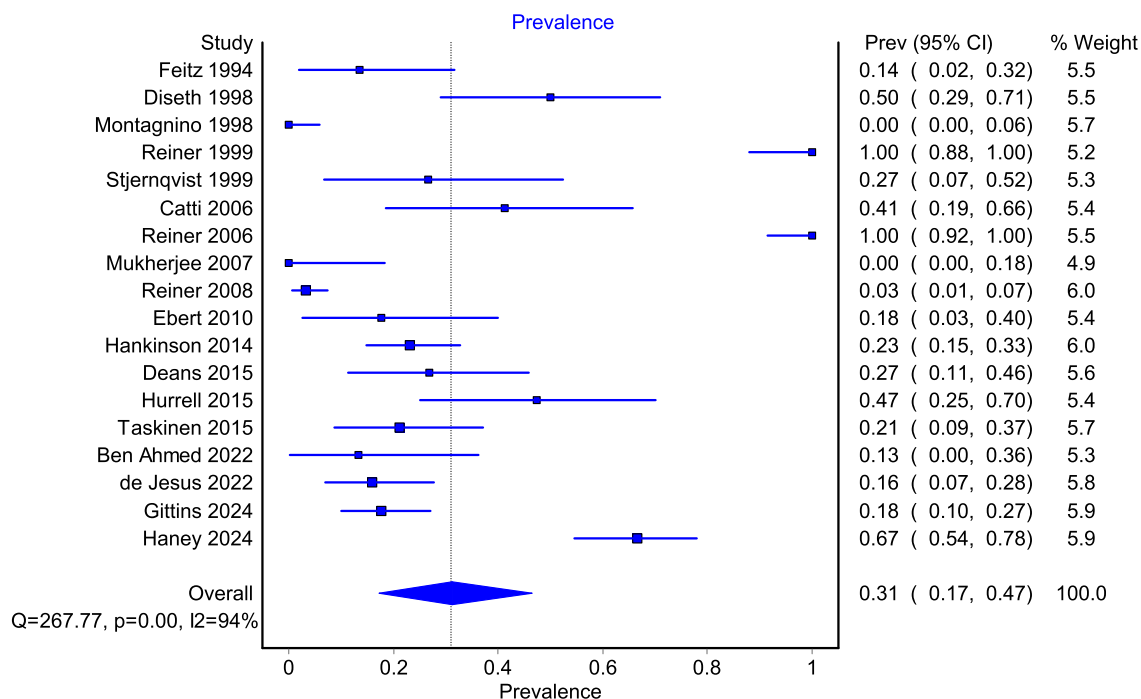


Fig. 2 Prevalence of psychiatric diagnosis or symptoms in bladder exstrophy and epispadias patients.

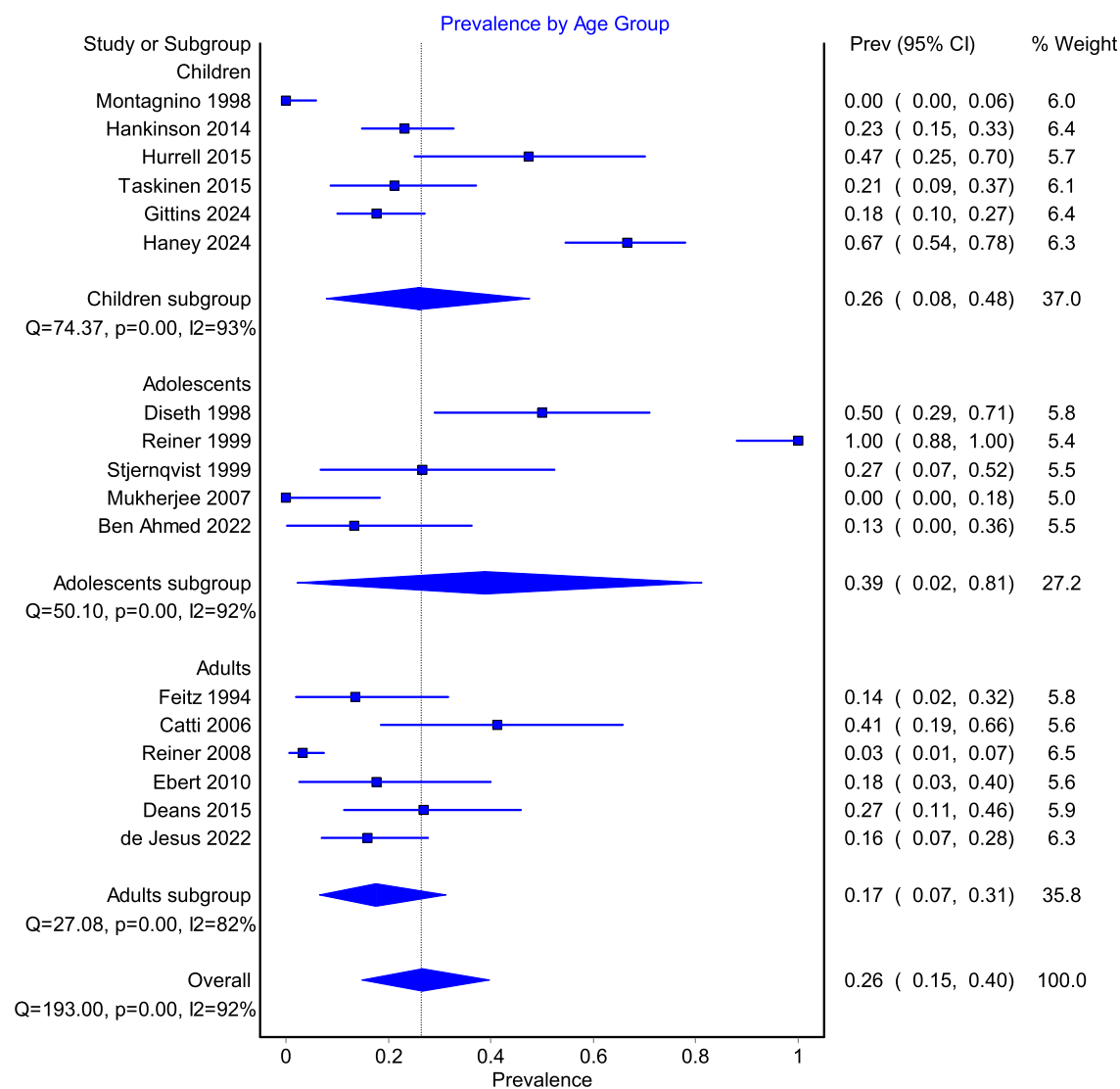


Fig. 3 Prevalence of psychiatric diagnosis or symptoms by age group in bladder exstrophy and epispadias patients.

Prevalence was 29 % [95 % CI 3 %–63 %] for the bladder exstrophy subgroup and 27 % [95 % CI 0 %–100 %] for cloacal exstrophy.

National registry results

We identified 57 patients diagnosed with BEEC from the registries, and 20 of these were included as true BEEC, five with primary epispadias, and 15 with bladder and cloacal exstrophy. Nine patients (45 %) were female, and 16 patients (80 %) had at least one psychiatric diagnosis.

All 16 patients were first diagnosed in childhood (<13 years). The most common psychiatric condition was unspecified behavioral syndrome associated with physiological disturbances and physical factors (F59), accounting for 12 diagnoses. The nature of the collected data available in the registry does not allow for more specific detailing on the type of behavioral symptoms. Neurodevelopmental disorders were also common, with five patients having at least one diagnosis, such as ADHD or Asperger syndrome.

Eight patients had only one psychiatric diagnosis, while the remaining eight had two to eight psychiatric diagnoses. Ten patients had other congenital malformations in addition to BEEC. In the control group, the most common psychiatric diagnosis groups were depression (n = 6), anxiety (n = 5), ADHD (n = 4) and sleep disorder (n = 4).

Sixteen out of 20 children with BEEC (80 %) had at least one psychiatric diagnosis, compared to 21 out of 80 (26 %) in the control group (OR 11.2, [95 % CI 3.37–37.4], $p < 0.001$). There was no significant difference in the prevalence of psychiatric diagnoses between epispadias patients (80 %) and patients with bladder or cloacal exstrophy (80 %), $p = 1.00$.

The most common diagnosis F59 'Unspecified behavioral syndrome associated with physiological disturbances and physical factors' could not by default be found in the control group to the same extent, as congenital anomalies were excluded. When excluding BEEC patients with F59 as their only psychiatric diagnosis, nine out of 20 subjects with BEEC had a psychiatric diagnosis, with OR 2.29, [95 % 0.83–6.32], $p = 0.1069$.

In multivariate analysis of risk factors affecting the rate of psychiatric morbidities in BEEC patients, controlling for maternal psychiatric morbidity and unemployment slightly reduced the OR to 10.8, [95 % CI 3.10–38.0], $p < 0.001$. However, neither maternal psychiatric diagnosis (OR 2.41, [95 % CI 0.89–6.55], $p = 0.085$) nor maternal unemployment (OR 1.12, [95 % CI 0.30–4.23], $p = 0.86$) was independently significantly associated with psychiatric morbidity in children with BEEC. Additionally, the number of surgeries was not significantly associated with psychiatric morbidity in BEEC patients in univariate analysis (OR 0.90, [95 % CI 0.78–1.03], $p = 0.13$).

Discussion

Our study reveals a substantial psychiatric burden among BEEC patients, with adolescents and young adults being particularly affected. The systematic review identified a psychiatric morbidity prevalence of 31 % overall, with a rate of 39 % among adolescents. At the same time, the national registry study demonstrated that 80 % of BEEC patients received a psychiatric diagnosis, an 11-fold increased risk compared to matched controls. These findings underscore the need for targeted mental health support during pivotal developmental periods characterized by identity formation and increasing independence.

Our registry results suggest that the inherent challenges of living with BEEC, rather than the severity of the anomaly, the number of surgical interventions, or maternal factors such as unemployment or psychiatric morbidity, primarily drive the observed psychiatric burden. The number of surgeries was not statistically significantly associated with psychiatric morbidity. This is likely because psychiatric diagnoses were prevalent in a large proportion of BEEC patients, limiting the ability to detect differences based solely on surgery count.

In contrast to previous literature that has focused mainly on surgical outcomes, continence, sexual function, and fertility, our results indicate that the chronic nature of BEEC significantly impacts mental health [2,4]. Moreover, in a published study, it was suggested that social factors, such as bullying and concerns about sexual relationships, may further contribute to the elevated psychiatric morbidity observed during adolescence [24]. Additionally, urinary incontinence has been linked to increased psychiatric symptoms in children and lower health-related quality of life in BEEC patients [21,25,26].

Our results indicate that the high prevalence of psychiatric morbidity in the Finnish BEEC population may be due to the high medical stress of BEEC and possibly because of genetic factors relating to BEEC. We also recognize that this patient group is followed intensely throughout their childhood and youth. Some behavioral issues that would be considered age-appropriate in a healthy individual and would go unnoticed may be diagnosed as psychiatric issues related to BEEC with these patients, due to regular assessments.

Behavioral symptoms as a reaction to any stress are commonly observed in childhood [27]. In our cohort, 55 % of BEEC patients were diagnosed with an “unspecified behavioral syndrome associated with physiological

disturbances and physical factors,” a diagnosis not observed in the control group. This non-specific diagnosis may not have been set based on pediatric psychiatric evaluation, but could instead reflect behavioral symptoms as a reaction to a debilitating chronic condition or medical stress experienced during childhood. When excluding the diagnosis of behavioral syndrome related to physiological factors as the only psychiatric diagnosis, the odds of having any psychiatric diagnosis remained more than twofold higher among BEEC patients compared with controls (OR 2.29), although the confidence interval was wide and the association did not reach statistical significance. This likely reflects limited statistical power due to the small cohort size rather than the absence of an underlying association.

In clinical practice, F59 is often used to describe behavioral symptoms occurring in the context of complex somatic conditions rather than as a discrete psychiatric disorder. This can be perhaps attributed partly to the practices in child psychiatry, where these types of diagnoses are often used to describe the intertwining of symptoms as related to a broader context and interaction rather than as a problem related to the child alone. It is also possible that symptoms that might receive a more specific psychiatric diagnosis in otherwise healthy children are more readily attributed to the underlying condition in BEEC patients, contributing to the frequent use of this code. Consistent with this interpretation, neurodevelopmental disorders were also commonly observed in our BEEC cohort, in line with previous literature showing associations between congenital malformations and neurodevelopmental conditions, likely reflecting shared mechanisms [28]. This advocates for screening for neurodevelopmental disorders in childhood for BEEC patients to facilitate early recognition and adequate support.

Adolescence appears to be a particularly vulnerable period for BEEC patients. Our review findings indicate that adolescents experience more psychiatric symptoms than children, with adults displaying the lowest rates of psychiatric diagnoses. This same trend has been observed in the age of onset of mental disorders in the general population as well [29]. However, BEEC patients can be in an especially vulnerable position at the onset of puberty, when factors such as sexuality and body image gain prominence. As teens increasingly seek normalcy, deviations in appearance or function, such as incontinence or atypical genital appearance, can heighten anxiety and lower self-esteem. Difficulties in sexual health have been documented in BEEC patients [3,14,22,26]. These challenges may further compound the psychological burden during adolescence. Although mood fluctuations are a normal part of adolescent development, the presence of a chronic condition like BEEC may amplify these challenges. Our quantitative analysis further indicates that psychiatric morbidity decreases in adulthood, aligning with reports that adult BEEC patients are generally well-adjusted and have prevalence rates of psychiatric morbidity comparable to the general population [4,30].

Literature supports our findings and provides additional insights into the mental health challenges BEEC patients face. SooHoo et al. (2024) conducted a scoping review and observed that while quality of life may improve following certain continence surgeries, adolescents with BEEC often

face increasing concerns about self-image and emotional well-being as they grow older [31]. Similarly, Gittins et al. (2024) found that BEEC patients screened for psychosocial difficulties at a multidisciplinary outpatient clinic showed elevated challenges across several psychosocial domains, particularly in recent years [23]. Their findings suggest that systematic psychosocial screening can help identify at-risk patients early and guide appropriate interventions. Furthermore, a systematic review by Dellenmark-Blom et al. demonstrated that BEEC is associated with diminished mental and social health-related quality of life, with urinary incontinence frequently identified as a key factor [13].

Our dual approach offers a comprehensive look into this complex topic. The systematic review grasps the spectrum of the literature and methodologies used, while the registry study reaches individuals with the diagnosis. The discrepancies between our two methodological approaches likely reflect inherent differences in study design. As a cohort study, the national registry-approach captures cumulative psychiatric diagnoses over 16–22 years, whereas most studies in the review were cross-sectional, assessing only current symptoms.

Limitations

We observed substantial heterogeneity in study methodologies in the systematic review. Of the 12 studies that used psychiatric questionnaires, only three were standardized tests directly targeting a specific psychiatric diagnosis: BAI, BDI-II and HADS. Other questionnaires were aimed at recognizing more general psychopathology or behavioral symptoms. Studies that used quality-of-life questionnaires used mainly the standardized SF-36 questionnaire and were more straightforward to combine. Quantitative synthesis on such varying methodologies in a meaningful manner is challenging and can skew the results. We, however, chose to include different types of studies despite the broad methodology, enabling us to include enough studies on a rare anomaly.

The rarity of BEEC also contributes to our limited sample size, despite reliable electronic registry data covering all BEEC diagnoses made in Finland over a six-year period. Moreover, the registry data was not verified through individual patient notes, which raises the possibility of misrecorded diagnoses. We interpreted the data to exclude all likely inaccurate BEEC diagnoses, however, this approach may have inadvertently excluded some true BEEC patients as well. Additionally, registry data also excludes individuals with psychiatric symptoms who do not meet diagnostic criteria or who do not contact the health care system.

Conclusions

Our findings demonstrate that BEEC is associated with a significantly elevated risk of psychiatric morbidity, particularly among adolescents and young adults. The consistent findings across both our approaches emphasize the need for screening for neurodevelopmental disorders and psychiatric symptoms and targeted mental health interventions with

sustained multidisciplinary support for BEEC patients and their families.

Ethics

This study was approved by Finnish Institute for Health and Welfare and the anonymity of the final results were approved by Findata.

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None.

Conflict of interest

The authors have no conflicts of interest to disclose.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.jpuro.2026.105795>.