

## Adulthood Urge Incontinence: Is Childhood Nocturnal Enuresis A Risk Factor?

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### ABSTRACT

Urge incontinence and childhood nocturnal enuresis are two related urinary conditions that significantly affect individuals and their quality of life, varying prevalence between age and obesity. This systematic review examines the literature on the relationship between childhood nocturnal enuresis and urge incontinence in adulthood, including the potential mechanisms linking these conditions. Ten studies met the inclusion criteria and were included in the review. The results showed a consistent association between childhood nocturnal enuresis and urge incontinence in adulthood. The pooled analysis demonstrated that childhood nocturnal enuresis was a risk factor for adult urge incontinence, with odds ratios ranging from 1.75 to 2.7. This relationship's potential mechanisms include nocturnal polyuria, detrusor overactivity, and arousal thresholds. However, the exact mechanisms still need to be fully understood and further investigated. Clinical implications of these findings suggest the importance of early identification and intervention for childhood nocturnal enuresis to potentially reduce the risk of developing urge incontinence in adulthood. Future research should focus on longitudinal studies to better understand the association between these conditions and explore potential risk factors and preventive strategies. Overall, this review highlights the need for increased awareness and management of childhood nocturnal enuresis to minimize the socioeconomic burden and improve the outcomes for individuals with urge incontinence.

**Keywords:** urge incontinence; childhood enuresis; complications; risk factors; pathophysiology; future directions; prognosis

### INTRODUCTION

Urge incontinence is a type of urinary incontinence seen in adults, which involves a sudden urge to void and results in involuntary urine leakage. This is a severe and debilitating condition with a social stigma attached. Early diagnosis, treatment, and referral concepts must be widely practiced among clinicians to avoid this condition's substantial socioeconomic burden and high morbidity.

Approximately 40% of people assigned female at birth (AFAB) and 30% of people assigned male at birth (AMAB) experience urge incontinence at some point. The prevalence of urinary incontinence varies mainly with age and obesity.

Other factors associated with urinary incontinence of different subtypes include previous hysterectomy or pelvic surgery, parity, pulmonary disease, diabetes mellitus, dementia, or residing in a nursing home [1].

Nocturnal enuresis, also known as "bed wetting," is a disorder in which episodes of urinary incontinence (uncontrollable leakage of urine) occur during sleep in children  $\geq 5$  years of age. Nocturnal enuresis can be present with or without lower urinary tract (LUT) symptoms. Nocturnal enuresis is not benign; it has severe repercussions for the child and the family.

Children are often punished and are at risk for physical and emotional abuse. Many children become isolated, lack self-esteem, and have poor academic performance. This activity highlights a detailed understanding of this prevalent yet misdiagnosed condition [2].

Nocturnal enuresis is subdivided into 2 categories;

1. Primary enuresis which is the presence of enuresis in a child  $\geq$  five years old who has never achieved an asymptomatic period ( $\geq 6$  months) of consistent nighttime dryness. It is often associated with a familial history of delayed urinary bladder control.
2. Secondary enuresis defined as the presence of enuresis in a child  $\geq$  five years old who has achieved an asymptomatic period ( $\geq 6$  months) of consistent nighttime dryness in the past. Secondary enuresis is triggered by an unusually stressful life event significant enough to cause psychosocial regression [3]. It may also be due to urologic and neurological problems, disorders of the spinal cord, and recurrent urinary tract infections.

A study by Bakhtiar K et al. identified that the prevalence of childhood nocturnal enuresis is higher in boys than girls [4]. However, this study aims to find the relationship between childhood nocturnal enuresis (CNE) and development of urge incontinence in adulthood.

**MATERIALS AND METHODS**

C.O. and other co-authors carried out a data search on PubMed, Google Scholar, and Cochrane using the keywords: childhood, nocturnal enuresis, adulthood urge incontinence, risk factors, and complications. These keywords were combined using the BOLEANS 'AND' or 'OR.'Articles collected were transferred to an Excel sheet, and those meeting the eligibility criteria were moved to Endnote.

**• Eligibility criteria**

The studies used in this article were selected based on the number of human participants, the aim of the study, and the results of the study.

**• Inclusion criteria**

Due to lack of data, articles published between 2004 to 2023 that had adults (18 years and older) diagnosed with urge incontinence and/or childhood enuresis (nocturnal and/or diurnal) with childhood enuresis defined as nocturnal and diurnal incontinence during childhood (up to age 18) and urge incontinence defined as the involuntary leakage of urine associated with a sudden, strong desire to void that cannot be delayed were used for this review. Studies with adequate sample size to provide sufficient statistical power for analysis and had to be observational (cohort, case-control, cross-sectional) or interventional (randomized controlled trials) study designs were used for our study.

**• Exclusion criteria**

Studies that did not meet the above criteria were excluded. Additionally, studies with a high risk of bias were excluded. Studies were assessed for risk of bias using appropriate tools such as the Cochrane Risk of Bias tool for randomized controlled trials and the Joanna Briggs Institute (JBI) critical appraisal checklist for observational studies. Studies that only examine other types of incontinence (e.g., stress incontinence, overflow incontinence), studies that include pediatric populations (age less than 18 years), studies that are case studies, case reports, or editorials, and studies with a small sample size (less than 10 participants) were also be excluded.

**• Search strategy and data extraction**

In consultation with electronic databases, PubMed, Google Scholar, and Cochrane were searched for relevant studies from articles published in the English Language. The references of review articles and included original publications were also screened for potentially relevant studies. Table 1 shows the search strategies used in the databases mentioned above.

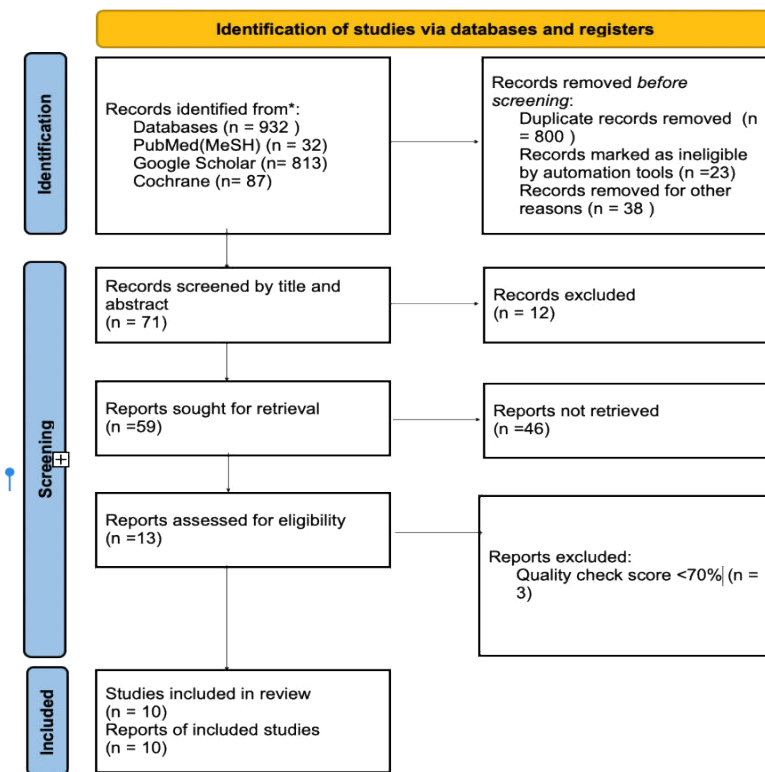
We followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) with the associated flow chart to report the numbers of included and excluded studies at each stage [7].

Table 1 below shows the search strategy employed, while Figure 1 shows the PRISMA flowchart.

**TABLE 1:** showing search methods, databases consulted, and number of articles per database.

Search Strategy	Database	Number of articles
("Nocturnal Enuresis/complications"[Majr: NoExp] OR "Nocturnal Enuresis/etiology"[Majr: NoExp] OR "Nocturnal Enuresis/physiopathology"[Majr: NoExp]) ("Urinary Incontinence, Urge/etiology"[Majr:NoExp] OR "Urinary Incontinence, Urge/physiopathology"[Majr: NoExp] )	PubMed (MeSH)	32
childhood nocturnal enuresis and Adulthood urge incontinence, nocturnal OR enuresis OR Adulthood OR urge OR incontinence	Google Scholar	813
Childhood enuresis OR Adulthood urge incontinence	Cochrane	87

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only



**FIGURE 1:** PRISMA 2020 flow chart showing data extraction methods. **PRISMA:** Preferred Reporting Items for Systematic Reviews and Meta-analysis.

**• Quality assessment**

The quality assessment was conducted separately for each study included in the systematic review, using appropriate tools such as the Cochrane Risk of Bias tool for randomized controlled trials and the Newcastle-Ottawa Scale for observational studies. Disagreements were resolved by consultation with the co-authors. Below is Table 2 with a summary of the quality appraisal tools used for all articles included in this review.

Quality appraisal tool summary. The accepted score percentage was set at 70.

SANRA (Minimum score 9 out of 12), AMSTAR 2 checklist (Minimum score 12 out of 16), JBI Critical Appraisal Checklist (Minimum score 6 out of 8), Cochrane Risk of Bias Assessment Tool (>= 7 out of 9).

AMSTAR: Assessment of Multiple Systematic Reviews.

SANRA: Scale for the Quality Assessment of Narrative Review Articles.

JBI Critical Appraisal Checklist: Joanna Briggs Institute Critical Appraisal Checklist.

**TABLE 2:** Quality Appraisal Tool Summary.

Author and Publication Year	Study Type	Quality Appraisal Tool	Score
Sidutu et al., 2019 [6]	Observational Study	JBI	6
Gong et al., 2022 [7]	Systematic Review and Meta-Analysis	AMSTAR	14
Fitzgerald et al., 2006 [8]	Retrospective Cohort	JBI	6
Kuh et al., 1999 [9]	Prospective Cohort	JBI	7
D’Ancona et al., 2012 [10]	Retrospective Cohort	JBI	6
Othman et al., 2020 [11]	Systematic Review	AMSTAR	13
Alkis et al., 2020 [12]	Literature Review	SANRA	11
Ciftci et al., 2012 [13]	Randomized Study	Cochrane Bias Assessment Tool	7
Foldspang and Mommsen, 1994 [14]	Cross-sectional Study	JBI	6

**RESULTS**

Our initial search for publications fetched 932 articles. After removing duplicates, and articles marked ineligible by the automation tool, 71 articles were left for screening. 59 articles were selected after sorting through titles and abstracts. 46 articles could not be retrieved such that 13 passed for eligibility criteria check using appraisal tool.

10 studies passed the quality check and were included in this study. A total of 53,247 participants consisting mainly of women ages 25 to 64. The pooled analysis showed that childhood nocturnal enuresis was consistently associated with urge urinary incontinence in adulthood.

**STUDY CHARACTERISTICS****TABLE 3:** Summary of articles included in this review.

Author and Publication Year	Study Type	Study Aim	Number of Participants	Study Results	Conclusion	Another outcome measured
Sidutu et al., 2019 [6]	Observational Study	To determine if enuresis is a risk factor for incontinence	285	34% of participants diagnosed with incontinence had initial symptoms of childhood enuresis, most of which were by age ten years. More than 50% of these were males, and more than 70% resided in urban areas.	About one-third of the people with nocturnal enuresis developed incontinence at an early age. There was an association with them living in the metropolitan area	The effect of behavioral, psychological, and infectious factors on the prevalence of overactive bladder
Gong et al., 2022 [7]	A systematic review and Meta-analysis	Determine the relationship between nighttime bed wetting and adulthood nocturia and summarize common risk factors.	26,070	A strong link between childhood enuresis and adult nocturia existed with an OR: 1.75 and at a 95% CI (1.11–2.40)	The research results suggest that experiencing childhood nocturnal enuresis significantly increases the likelihood of developing nocturia in later stages of life.	They investigated the effect of aging, genetics, and obstructive sleep apnea and its association with childhood nocturnal enuresis.
Fitzgerald et al., 2006 [8]	Retrospective Cohort	Explored the correlation between urinary symptoms experienced during childhood and those observed in middle-aged women.	2,106	A significant correlation was observed between frequent nocturia during childhood and adult nocturia (odds ratio [OR] 2.3, 95% confidence interval [CI] 1.5-3.5, $p < 0.001$ ). Moreover, childhood daytime incontinence was found to be associated with adult urge incontinence (OR 2.6, 95% CI 1.1-5.9, $p < 0.05$ ), as well as childhood nocturnal enuresis (OR 2.7, CI 1.3-5.5, $p < 0.01$ ).	There was a significant association found between childhood urinary symptoms and urinary tract infections (UTIs) with adult overactive bladder symptoms.	The role of current estrogen levels, history of hysterectomy, diabetes, BMI, and race as it relates to Adulthood urinary incontinence.

Author and Publication Year	Study Type	Study Aim	Number of Participants	Study Results	Conclusion	Another outcome measured
Kuh et al., 1999 [9]	Prospective cohort	The effect of childhood enuresis and other risk factors on urinary incontinence in middle-aged women	1333	The study showed that 50% of the participants reported symptoms of incontinence in the past 12 months, of which 8% had severe symptoms, 15% and 32% had moderate and mild symptoms respectively	It was shown that women who had regular day and night time urinary symptoms in childhood were 1.5X more likely to suffer urge incontinence in adulthood.	The association between delivery after 30 years and stress urinary incontinence
D'Ancona et al., 2012 [10]	Retrospective cohort	Relationship between childhood enuresis and bladder dysfunction in adulthood	661	The presence of childhood enuresis in childhood was more likely to be associated with urge incontinence compared to stress incontinence with an odds ratio of 2.37 and confidence interval of 1.43-3.92. When compared to stress urinary incontinence, women with mixed urinary incontinence were more likely to have a history of childhood enuresis with OR: 1.77 CI: 1.15-2.73	Individuals with a history of mixed urinary incontinence and stress urinary incontinence are more likely to have a history of childhood urinary incontinence	The relationship between stress urinary incontinence and mixed urinary incontinence in individuals with a history of childhood urinary incontinence.
Othman et al., 2020 [11]	Systematic review	Is childhood nocturia as a risk factor for pelvic floor disorder and urinary tract symptoms in women	20,000	There was a strong association between childhood nocturnal enuresis and mixed urinary incontinence with OR: 2.62 CI: 2.03-3.40	Childhood enuresis is significantly linked to mixed urinary incontinence.	Pelvic floor disorder and lower urinary tract symptoms
Alkis et al., 2020 [12]	Literature review	Factors involved in the presentation of overactive bladder in adults with a history of childhood voiding disorder	144	While looking to see if daily water, tea and coffee consumption, cigarette smoking and alcohol consumption in both groups were risk factors to development of OAB, there were no statistically significant difference found. However, a significant difference was found in the obese participants and those who consumed hot chilli.	The study showed that the consumption of hot chili and obesity is a risk factor for the development of overactive bladder in adulthood in participants with childhood voiding disorders.	Daily water, tea and coffee consumption, smoking and alcohol use were not risk factors to the development of OAB in participants who had childhood voiding disorders.

Author and Publication Year	Study Type	Study Aim	Number of Participants	Study Results	Conclusion	Another outcome measured
Ciftci et al., 2012 [13]	Retrospective randomized study	Association between childhood enuresis and nocturnal polyuria syndrome in adulthood	35	A notable correlation was observed between childhood nocturnal enuresis and adult nocturnal polyuria.	The study concluded that men with a history of childhood enuresis had a higher risk of adulthood nocturnal polyuria syndrome.	-
Foldspang and Mommsen, 1994 [14]	Cross-sectional study	Relationship between incontinence in females and bedwetting in childhood	2613	Childhood bedwetting was shown to be associated with 14.7% of stress incontinence, 8.3% of urge incontinence and 6.8% of mixed incontinence.	It was concluded that incontinence in childhood was correlated with urge incontinence in Adulthood.	Nocturnal enuresis and incontinence during anxiety
Selvi I, et al., 2021 [15]	Retrospective cohort study	To analyze if a relationship exists between childhood lower urinary tract symptoms and adulthood overactive bladder.	264	38.6% of patients recovering from lower urinary tract symptoms had terrible overactive bladder and quality of life in their adulthood compared to those without lower urinary tract symptoms.	It was concluded that children with lower urinary tract symptoms are at an increased risk of developing overactive bladder later in their lives, regardless of whether their symptoms improved in childhood.	To evaluate the effect of the history of childhood lower urinary tract symptoms on the quality of life in adulthood.

## DISCUSSION

### • Possible mechanisms of how childhood nocturnal enuresis could lead to urge incontinence

The literature reveals that childhood nocturnal enuresis (CNE) originates from a complex mix of environmental, psychological, genetic, and neurologic factors [6]. Studies also show that people who suffer childhood enuresis are likely to develop urge incontinence in Adulthood [7]. Most studies focus on the similarities of childhood nocturnal enuresis, urge incontinence, and dissimilarity. Details of the exact mechanisms are not commonly expounded in literature.

Few studies postulate that childhood nocturnal enuresis and urge incontinence are linked by three mechanisms that mark the neurologic cause of childhood nocturnal enuresis. These mechanisms begin in childhood and continue into Adulthood. These include nocturnal polyuria, detrusor overactivity, and arousal thresholds [8]. These mechanisms are likely linked to an underlying brainstem pathophysiology. Children who suffer from enuresis are thought to produce a large amount of urine at night [9].

This is possible because of a decrease in the production of antidiuretic hormone (ADH), known to modulate water resorption in the kidneys to yield more concentrated urine [10]. Therefore, the absence or insufficiency of ADH due to any cause would result in increased urine production, leading to enuresis. It is explained that the same ADH pathophysiology leads to nocturnal polyuria, which could manifest as urge incontinence in an adult [11]. This seems to be due to a transition of the childhood developmental insufficiency of ADH to ineffective diurnal secretion of ADH in Adulthood [12]. Perhaps it points to the usefulness of desmopressin as a treatment in some cases of enuresis and polyuria. Sudui et al. postulate that this pathophysiology might be due to an anatomical defect between the locus coleres and the adjacent micturition center, which also makes neural connections to the hypothalamus where ADH is produced [13]. Since the locus querulous is located in the mesencephalon, which contributes to wakefulness, it seems logical that an anomaly in the structure of this area could impact the functional relationship and may lead to childhood nocturnal enuresis and, eventually, adult urge incontinence.



Other studies suggest CNE could lead to urge incontinence due to poorly established childhood circadian rhythm [14]. Children with delays developing an established circadian rhythm could have poor bladder wall control. This often leads to low nighttime bladder volume and increased bladder wall contraction with symptoms such as detrusor overactivity and urge incontinence in adulthood [16].

Despite the link and similarities, these studies agree that the arousal mechanism is the one dissimilar factor between enuresis and urge incontinence. It appears that children who suffer enuresis sleep more deeply and have poor arousal, which leads to bedwetting [15]. Asleep, they are unaware of the physiologic indicators of a full bladder. On the other hand, adults who suffer urge incontinence seem to have appropriate arousal from a full bladder.

#### • Evidence for a causal relationship between childhood nocturnal enuresis and urge incontinence

This systematic review explores the available data for a causal relationship between childhood nocturnal enuresis and urge incontinence. In a population-based cohort study by Sidutu et al., it was found that 34.38% of individuals diagnosed with an Overactive Bladder (OAB) had previously suffered from nocturnal enuresis. This statistical analysis suggests a pathophysiological relationship between these two conditions. Furthermore, a significant fraction of patients (75.51%) came from an urban environment, indicating that social, professional, and nutritional urban factors could trigger OAB [6]. A meta-analysis conducted by Gong et al. assessed the association between childhood nocturnal enuresis and adult nocturia, involving 26,070 participants across eight studies. This collective 'random effects' model demonstrated a notable association between childhood nocturnal enuresis and nocturia, with an (OR 1.75, CI: 1.11–2.40). The meta-analysis further supports the relationship between childhood nocturnal enuresis and urinary symptoms in adulthood [7].

Longitudinal studies have provided valuable insights into the relationship between childhood nocturnal enuresis and urge incontinence. A prospective study by Fitzgerald et al. involving older and middle-aged women from America showed that childhood nocturnal enuresis was associated with two times more risk of urge incontinence in adulthood (OR 2.7, 95% CI 1.3-5.5) [8]. Similarly, a prospective study of British women by Kuh et al. revealed that 22.3% of individuals involved in the study who experienced childhood enuresis had developed urge incontinence by age 48 [9].

The relationship between childhood enuresis and Nocturnal Polyuria Syndrome (NPS) was investigated by Cifciti et al. and the study demonstrated that individuals with childhood enuresis were more likely to develop NPS. A clear correlation ( $p < 0.0001$ ) was also noticed between late childhood nocturnal enuresis and adult urinary incontinence, especially during sleep [13]. This finding suggests that a pattern of nocturnal incontinence could persist for several years in these individuals. Therefore, the link between childhood enuresis to urge incontinence and nocturnal polyuria syndrome could significantly decrease the quality of life for individuals with a history of childhood enuresis who develop both NPS and urge incontinence in adulthood.

According to a study by Othman et al., pelvic floor disorders were significantly more common in nulliparous women with a history of nocturnal enuresis in childhood [11]. This raises the possibility of a shared factor connecting adult pelvic floor disorders and childhood nocturnal enuresis.

It could be argued, however, that childhood nocturnal enuresis is not the single most predicting factor amongst other urinary tract symptoms in childhood for the development of an overactive bladder in adulthood. Results from this study showed that daytime incontinence (OR 2.01), holding maneuvers (OR 1.82), and avoiding Dysfunction Symptom Score  $\geq 13$  (OR 2.54) were higher determinants than pediatric nocturnal enuresis (OR 1.75) [15]. However, this does not refute the relationship between these two disorders. Epidemiological research, meta-analyses, longitudinal studies, investigations into related pelvic floor issues, and lower urinary tract symptoms have all repeatedly shown that these two disorders are related.

#### • Implications for clinical practice and future research directions

The prevalence of CNE and urge incontinence in adulthood calls for early identification, intervention, and preventive strategies [17]. These are essential to reduce risk. Healthcare providers can give counseling and education to patients with enuresis, emphasizing healthy bladder training and lifestyle modifications. This will empower individuals to manage their bladder health and reduce the risk of future incontinence and psychological and behavioral problems [9]. The management of the conditions can be customized based on the underlying cause in each patient, and closely monitoring the treatment is pivotal for a successful outcome. Early identification and treatment of CNE, preferably before the age of 6 years, are ideal. Moreover, considering the patient's and family's motivation is crucial in determining any intervention's success [18]. Gong et al. also pointed out the importance of identifying and addressing any cause of psychological stress in children to prevent the progression of CNE to adulthood [7]. For urge incontinence, many individuals undergoing treatment do not achieve a cure and may still depend on containment strategies, including behavioral approaches and the use of containment products [19]. This emphasizes the need for a multidisciplinary management approach in the adult population.

Considering that most of the studies used in this review depended on what the patients could recall, we recommend that for future research, longitudinal studies that follow individuals from childhood to adulthood can provide valuable insights into the association between childhood enuresis and adulthood urge incontinence as these studies will help identify potential risk factors or protective factors. Also, exploring factors like bladder dysfunction, hormonal changes, genetic predisposition, and psychological factors could help reveal the physiological, neurological, and psychological relationships between these conditions. Comparative studies should also explore the impact of different early intervention treatment approaches for childhood enuresis, such as behavioral therapies, medication, or combination treatments, on the long-term outcomes of reducing the risk of adult urge incontinence.

#### STRENGTHS AND LIMITATIONS

The primary strength of this review lies in its comprehensive search across a diverse range of populations, databases, and open-access registers to ensure relevance and inclusiveness. The major limitation encountered is a lack of data and studies on this topic, highlighting the need for more longitudinal studies.

#### CONCLUSION

There is a relationship between childhood nocturnal enuresis and the development of urge incontinence in adulthood. Details of the exact mechanisms still need to be fully understood.

However, it is considered a combination of environmental, psychological, and genetic factors and the common neurologic origin the conditions share. A considerable percentage of adults suffer from urge incontinence at some point. Currently, limited research is available on the relationship between childhood nocturnal enuresis and urge incontinence, elucidating the necessity for more studies on the subject matter. Investigating possible predisposing factors to urge incontinence, such as childhood nocturnal enuresis, could therefore point toward more informed and intentional management of children with nocturnal enuresis. Guidelines could be established to limit the sequelae of incontinence development.

**CONFLICTS OF INTEREST**

All authors declare no conflict of interest in this paper.

**FINANCIAL RELATIONSHIPS**

All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

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- (1) Making substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data.
- (2) Drafting the article or reviewing it critically for important intellectual content
- (3) Final approval of the version to be published and
- (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.