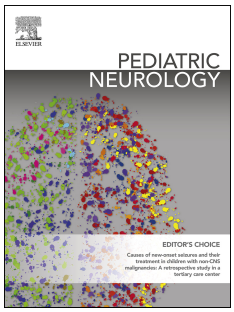

Febrile Seizures and Sudden Death Risk: A Case-Controlled Analysis

Laura Gould, MSc, Steven Friedman, MS, Thomas Wisniewski, MD, Orrin Devinsky, MD

PII: S0887-8994(25)00170-5

DOI: https://doi.org/10.1016/j.pediatrneurol.2025.06.004

Reference: PNU 10900

To appear in: *Pediatric Neurology*

Received Date: 19 November 2024

Revised Date: 1 May 2025

Accepted Date: 4 June 2025

Please cite this article as: Gould L, Friedman S, Wisniewski T, Devinsky O, Febrile Seizures and Sudden Death Risk: A Case-Controlled Analysis, *Pediatric Neurology* (2025), doi: https://doi.org/10.1016/j.pediatrneurol.2025.06.004.

Febrile Seizures and Sudden Death Risk: A Case-Controlled Analysis

Laura Gould, MSc
Department of Neurology, NYU Grossman School of Medicine, New York, NY, USA
NYU Comprehensive Epilepsy Center
223 East 34th St, New York, NY 10016

Steven Friedman, MS
Department of Population Health – Biostatistics Division, NYU Grossman School of Medicine, New York, NY, USA
180 Madison Ave, New York, NY, 10016

Thomas Wisniewski MD
Center for Cognitive Neurology, Department of Neurology, NYU Grossman School of Medicine, New York, NY, USA
Department of Psychiatry, NYU Grossman School of Medicine, New York, NY
Department of Pathology, NYU Grossman School of Medicine, New York, NY
145 E 32nd St 2nd floor, New York, NY 10016

Orrin Devinsky, MD
Department of Neurology, NYU Grossman School of Medicine, New York, NY, USA
NYU Comprehensive Epilepsy Center
223 East 34th St, New York, NY 10016

Corresponding Author:
Laura Gould
NYU Comprehensive Epilepsy Center
223 East 34th St, New York, NY 10016
laura.gould@nyulangone.org
P: 646-754-223

Abbreviations and Acronyms

Sudden Unexplained Death in Childhood (SUDC), Febrile Seizure (FS)

Abstract

Background: Febrile seizures occur in 3-4% of U.S. children 6 months to 5 years and are considered benign. However, Sudden Unexplained Death in Childhood is associated with 10x increase in FS. We assessed the characteristics of children with febrile seizure and sudden death to identify factors that confer increased sudden death risk.

Methods: We conducted a case-controlled analysis of children with febrile seizure and subsequent sudden death versus living controls from December 2021 to June 2023 through a ~10-minute anonymous online survey. We enrolled parents of children, living or deceased, whose child had experienced a febrile seizure from 6 months to 6 years. Subjects were excluded if the child had an afebrile seizure or parents had not witnessed a febrile seizure. Demographic characteristics, parasomnias and febrile seizure features were analyzed.

Findings: 381 completed surveys were received; 53 (14%) cases of febrile seizure with sudden death and 328 (86%) living controls. Cases experienced febrile seizure onset >2 months younger (p=.013), reported developmental concerns (OR= 2.32, CI95[1.14,4.71], p=.03), less frequent night awakenings (OR=.34, CI95[0.18,0.65], p=.001) and less restless sleep (OR=.37, CI95[0.16,0.85], p=.02). Cases were also less likely to drool (OR= .442, CI95[0.218,0.900] p=.032) or be unresponsive for > 1minute (OR= .45, CI95[0.238,0.854] p=.021).

Interpretation: We report novel associations of febrile seizure and sudden death related to age, development, sleep and observed ictal features. Anonymous survey methodology cannot exclude ascertainment bias and any related potential effect on results. Our findings suggest that impaired arousal mechanisms may increase risk of death in febrile seizure subjects.

Funding: This study was supported by SUDCUK, Finding a Cure for Epilepsy and Seizures (FACES) at NYU and UL1TR001445. TW is supported by P30AG066512 and P01AG060882.

Introduction

Febrile seizures (FS) are the most common pediatric convulsive event occurring in 3-4% of US children.[1,2] Considered largely benign, there are rare reports of sudden death that have parallels to sudden unexpected death in epilepsy (SUDEP).[3] Further, SUDEP risk factors, including death during sleep period found in bed in prone position, and male sex, are shared by toddlers who die suddenly and without a cause of death identified despite complete autopsy and forensic evaluation.[4] Such toddlers have a ten-fold increased incidence of febrile seizures and some without such a history have been found to have convulsive events immediately before death.[3] Among children with FS, we lack clinical or laboratory findings to identify those at higher risk for sudden death.

FS are provoked by fever or illness without an underlying central nervous system infection and typically affect children 6 months to 6 years.[5-7] Genetic and environmental risks are associated with susceptibility in the young developing nervous system.[8] Simple FS are generalized, <15 minutes, and do not recur in 24 hours; they account for 65-90% of FS.[9,10] Complex FS last >15 minutes, recur within 24 hours or have ictal or postictal focal features.[9,10] Febrile status epilepticus lasts >30 minutes as a continuous event or cluster without full recovery between seizures.[10] More than 25% of FS cases have a family history of FS or epilepsy.[11] FS symptoms include loss of consciousness, tonic and/or clonic movements affecting 1-4 extremities, and eye rolling. Care for simple FS involves identifying the source of fever but not working up the seizure.[8] EEGs do not predict FS recurrence.[12] When recurrent FS occur, especially if complex, many pediatric neurologists explore potential genetic causes (e.g., SCN1a variants), magnetic resonance imaging or prolonged EEGs.

Sudden unexplained death in childhood (SUDC) is the sudden death of a ≥ 12-month child, whose cause of death is unknown despite a thorough investigation.[13] SUDC affects ~400 United States children every year, with >31,000 life years lost annually.[14-16] SUDC is associated male predominance (59%), unwitnessed sleep related deaths (88%) and FS (30%); ~10x the incidence of the population.[17-20] Most SUDC are also 1-4 years old (55%); overlapping the peak FS incidence. Videos of the last sleep period of SUDC commonly identified terminal convulsions before death.[3]

While almost all SUDC occurs during sleep periods, sleep characteristics in SUDC are unknown. Such features may shed light on redisposition of risk or protection.

SUDC incidences have not changed in 20 years.[15] Our systematic review of brief FS identified child death registries that FS cases are more common than in controls, supporting a potential association of simple FS with increased mortality.[21] Pathogenic variants in cardiac and epilepsy genes are more common in SUDC cases than controls.[22,23] Since no risk identification measures distinguish children with FS at greater risk for sudden death, we evaluated FS features in children with and without sudden death to identify potential mortality risk among FS patients.

Methods

This study was approved by the NYU Langone Health Institutional Review Board and considered exempt with a waiver of documentation of informed consent. (i21-01294) The study's inclusion criteria included parents or legal guardians who witnessed a complete FS in their child since 2015 and whose child experienced their first FS between 6 months and 6 years of life. We excluded parents who did not witness the FS and children with a history of afebrile seizure.

The case-control research design collected data through an anonymous online (Qualtrics) survey including ~40 questions from 2 validated seizure interview tools and 1 parasomnia scale.[24-26] Cases were children who satisfied inclusion criteria but experienced sudden death; controls were living children with FS. Demographic characteristics of the parent subject who completed the survey were collected. Demographic characteristics, parasomnias and FS features were collected from all cases and controls. (Supplement 1)

The study was marketed to Pediatricians at NYU Langone Health, Yale University, Social Media groups (Facebook groups for "Pediatricians in Private Practices" and "Parents of Children with Febrile Seizures"), organizations supporting parents of sudden unexplained death in childhood (SUDC Foundation and SUDC-UK) and NYU MyChart Alerts for emergency department visits from 2015 to 2022 with primary complaint of FS. Due to the marketing strategy, the number of surveys received by subjects meeting inclusion criteria is unknown. The survey was open from December 1, 2021, to June 1, 2023.

Univariate analysis of demographic information, parasomnias and FS features were calculated using 2-tailed t-test for continuous variables (or, when the variances between groups were found to be unequal, the Welch test) and χ^2 test of independence for categorical variables, with significance differences at $p<.05$. Adjusted odds ratios (aOR) were calculated using logistic regression with SUDC vs. control as the binary response and sex, family history of FS, family history of epilepsy, restless sleep, waking twice, age at first FS, drooling, developmental concerns, duration of non-response, and time of day as covariates. We believe any missing observations are missing completely at random and we used multiple imputation (MICE package in R) on the entire dataset to replace missing values using predictive mean matching based on 10

imputations. Statistical analyses were performed using R (ver. 4.3.2). Data reporting follows the STROBE checklist for case-control studies.

Results

Among 381 valid completed surveys collected from December 1, 2022, to June 1, 2023, 53 (14%) were cases of FS with SUDC (FS+SUDC) and 328 living controls with FS (FS Only).

Overall, sixty percent of all respondents completed > 16 years of education and 96% were mothers. Surveys of cases were less likely to be completed by mothers and more likely referred by an organization rather than social media. Household income and education were similar among cases and controls. (Table 1)

Cases and controls were similar in regards to sex, race, first-degree family history of FS and epilepsy, but FS+SUDC were significantly younger at age of onset of FS (2.31 months CI95[0.50,4.12], p=.013) and over 2x more likely to report developmental concerns (OR= 2.32, CI95[1.14,4.71], p=.03; Table 2) The mean age of death of FS+SUDC cases was 27.5 months, and mean duration from FS onset to death was 10.8 months. (Table 3) The median age of controls at time of survey completion was 3-4 years of age.

FS+SUDC were less likely to be restless sleepers (13.2% FS+SUDC vs 28% FS Only, OR= .37, CI95[0.16,0.85], p=.024,) or awaken >2x per night often (28.3% FS+SUDC vs 49.7% FS Only, (OR= .34, CI95[0.18,0.65], p=.001. (Table 4)

FS characteristics and FS types witnessed throughout life were similar across cases and controls except for FS+SUDC were less likely to be unresponsive for $\geq$1min (OR= .45, CI95[0.24,0.85], p=.02), or drool (OR= .44, CI95[0.22,0.90]), p=.03) during the FS. (Supplement A)

After the adjustments and imputations, sudden death was still associated with never or occasionally waking more than twice during the night (aOR=3.5, CI95[1.32,9.08]) and not responding for <1 minute during the FS (aOR=0.34, CI95[0.14,0.85]). (Table 5)

Discussion

Our exploratory analysis of FS characteristics suggests an increase in sudden death risk related to early age of FS onset, development concerns, and parasomnias, as well as brief unresponsiveness (<1 minute) and absence of drooling during the FS. Further analysis identified that even after adjustment to other characteristics, FS+SUDC rarely awoke often (>2x) during the night, supporting possible differences in arousal mechanisms in children with FS and subsequent sudden death. Impaired arousal is implicated in SUDEP as a result of postictal generalized EEG suppression, a potential SUDEP biomarker, and as a feature that accounts for why many convulsive seizures are followed by full recovery in a patient but a subsequent convulsive seizure is fatal.[4] Thus, impaired arousal mechanisms may be shared among patients who die after FS and from SUDEP.

Most children with FS have favorable outcomes; the risk of sudden death is extremely low. [21] However, identification of seizure-related deaths in sleep when children are not observed is limited. Postmortem examinations and toxicology studies rarely provide supportive evidence in SUDC or in SUDEP cases even when a terminal seizure was witnessed. Thus, forensic evaluations underestimate the incidence of seizure- or epilepsy-related deaths. While some deaths support a possible terminal FS (e.g. history of FS, terminal febrile episode, infection, and found prone faced down), findings are not conclusive and histology, including neuropathology, is usually unremarkable.[18,20] In a large population based longitudinal study, children with FS had

increased mortality rates for seizure-related and "ill-defined" deaths (ICD R95-99)- an umbrella category to which deaths certified as sudden unexplained death in childhood are allocated.[27]

How do we identify the FS patient who is at increased risk of sudden death, a rare complication in patients with FS? Since most FS+SUDC cases have had simple rather than complex FS, the intuitive risk factor of seizure severity is not supported by the data. Patients with FS and impaired arousal mechanisms after FS with reduced sleep quality may be at higher risk. Our results suggest FS+SUDC may have a developmentally immature nervous system, and possibly reduced arousal mechanisms peri-ictally. Lower postictal arousal levels during a young child sleeping prone may create a perfect but tragic storm.

Some limitations decrease the potential generalizability of our results. Retrospective and recall bias is possible. We attempted to identify differences among cases versus controls in regard to recall and identified similar frequencies of "I don't know" responses suggesting there was not a difference in recall between groups. Our data relied on parental reports without confirmatory medical records. However, parent accounts of FSs are the norm in medical records, since convulsions have often terminated before access to medical care. The development concerns cited in our survey were nonspecific. Anonymous survey methodology cannot exclude ascertainment bias and any related potential effect on results. Finally, our limited number of FS+SUDC cases versus FS Only controls along with missing data may bias our findings.

Conclusions

Our novel associations of FS+SUDC related to age, development, sleep and observed ictal features reported by witnesses suggest that arousal mechanisms may play a role in FS-related deaths. Sudden unexplained child deaths warrant thorough investigations, including complete

autopsy with full neuropathology. Further research should include a large prospective cohort study of FS to confirm these potential risk factors and include specificity of development concerns and objective measurements of sleep quality with direct observations of FS characteristics.

Data Sharing

Survey available in Supplement 1. Data dictionary available upon request via email to laura.gould@nyulangone.org

Acknowledgements

This study was supported by SUDCUK and Finding a Cure for Epilepsy and Seizures (FACES) at NYU and the National Center for Advancing Translational Sciences (NCATS), National Institutes of Health, through Grant Award Number UL1TR001445. TW is supported by P30AG066512 and P01AG060882. The SUDCUK and FACES at NYU had no role in the design of the study. SUDCUK did share information about the study.

Contributor Statements and Conflicts of Interest Statements

Laura Gould conceptualized and designed the study, designed the data collection instruments, collected data, carried out the initial analyses, drafted the initial manuscript, and critically reviewed and revised and the manuscript. Dr Thomas Wisniewski and Dr Orrin Devinsky assisted in conceptualizing and designing the study, critically reviewing and revising the manuscript for important intellectual content. Steven Friedman provided statistical analysis and critical review and revision of manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work. None of the authors have any conflict of interest to disclose relevant to this study.

Ethics Approval

This study was approved by the NYU Langone Health Institutional Review Board and considered exempt with a waiver of documentation of informed consent. (i21-01294)

REFERENCES

1. Graves RC, Oehler K, Tingle LE. Febrile seizures: risks, evaluation, and prognosis. *Am Fam Physician*. Jan 15 2012;85(2):149-53.
2. Corsello A, Marangoni MB, Macchi M, et al. Febrile Seizures: A Systematic Review of Different Guidelines. *Pediatr Neurol*. Jun 2024;155:141-148. doi:10.1016/j.pediatrneurol.2024.03.024
3. Gould L, Reid CA, Rodriguez AJ, Devinsky O, for SVWG. Video Analyses of Sudden Unexplained Deaths in Toddlers. *Neurology*. Feb 13 2024;102(3):e208038. doi:10.1212/WNL.0000000000208038
4. Devinsky O, Hesdorffer DC, Thurman DJ, Lhatoo S, Richerson G. Sudden unexpected death in epilepsy: epidemiology, mechanisms, and prevention. *Lancet Neurol*. Sep 2016;15(10):1075-88. doi:10.1016/S1474-4422(16)30158-2
5. Oluwabusi T, Sood SK. Update on the management of simple febrile seizures: emphasis on minimal intervention. *Curr Opin Pediatr*. 2012;(1531-698X (Electronic))
6. National Institute of Neurological Disorders and Stroke N. Febrile Seizures Facts Sheet. NIH. Updated 6/16/2021. 2015. https://www.ninds.nih.gov/febrile-seizures-fact-sheet
7. Laino D, Mencaroni E, Esposito S. Management of Pediatric Febrile Seizures. *Int J Environ Res Public Health*. Oct 12 2018;15(10)doi:10.3390/ijerph15102232
8. Leung AK, Hon KL, Leung TN. Febrile seizures: an overview. *Drugs Context*. 2018;7:212536. doi:10.7573/dic.212536
9. Smith DK, Sadler KP, Benedum M. Febrile Seizures: Risks, Evaluation, and Prognosis. *Am Fam Physician*. Apr 1 2019;99(7):445-450.
10. Xixis KL, Samanta D, Smith T, Keenaghan M. Febrile Seizure. *StatPearls*. 2024.
11. Sartori S, Nosadini M, Tessarin G, et al. First-ever convulsive seizures in children presenting to the emergency department: risk factors for seizure recurrence and diagnosis of epilepsy. *Dev Med Child Neurol*. Jan 2019;61(1):82-90. doi:10.1111/dmcn.14015
12. Kuturec M, Emoto SE, Sofijanov N, et al. Febrile seizures: is the EEG a useful predictor of recurrences? *Clin Pediatr (Phila)*. Jan 1997;36(1):31-6. doi:10.1177/000992289703600105
13. Krous HF, Chadwick AE, Crandall L, Nadeau-Manning JM. Sudden unexpected death in childhood: a report of 50 cases. *Pediatr Dev Pathol*. May-Jun 2005;8(3):307-19. doi:10.1007/s10024-005-1155-8
14. Krous HF, Chadwick AE, Crandall L, Nadeau-Manning JM. Sudden unexpected death in childhood: A report of 50 cases. *Pediatric and Developmental Pathology*. 2005;8(3):307-319. doi:10.1007/s10024-005-1155-8
15. Centers for Disease Control and Prevention NCfHSNVSS. Mortality 2018-2021 on CDC WONDER Online Database, released in 2021. Data are from the Multiple Cause of Death Files, 2018-2021, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed Accessed at http://wonder.cdc.gov/ucd-icd10-expanded.html on Feb 2, 2023 9:06:20 PM.
16. Harowitz J, Crandall L, McGuone D, Devinsky O. Seizure-related deaths in children: The expanding spectrum. *Epilepsia*. Mar 2021;62(3):570-582. doi:10.1111/epi.16833
17. Crandall L, Devinsky O. Sudden unexplained death in children. *Lancet Child Adolesc Health*. Sep 2017;1(1):8-9. doi:10.1016/S2352-4642(17)30003-2
18. Crandall LG, Lee JH, Stainman R, Friedman D, Devinsky O. Potential Role of Febrile Seizures and Other Risk Factors Associated With Sudden Deaths in Children. *JAMA Netw Open*. Apr 5 2019;2(4):e192739. doi:10.1001/jamanetworkopen.2019.2739
19. Hefti MM, Kinney HC, Cryan JB, et al. Sudden unexpected death in early childhood: general observations in a series of 151 cases: Part 1 of the investigations of the San Diego SUDC Research Project. *Forensic Sci Med Pathol*. Mar 2016;12(1):4-13. doi:10.1007/s12024-015-9724-2

20. Crandall LG, Lee JH, Friedman D, et al. Evaluation of Concordance Between Original Death Certifications and an Expert Panel Process in the Determination of Sudden Unexplained Death in Childhood. *JAMA Netw Open*. Oct 1 2020;3(10):e2023262. doi:10.1001/jamanetworkopen.2020.23262
21. Gould L, Delavale V, Plovnick C, Wisniewski T, Devinsky O. Are brief febrile seizures benign? A systematic review and narrative synthesis. *Epilepsia*. Oct 2023;64(10):2539-2549. doi:10.1111/epi.17720
22. Halvorsen M, Gould L, Wang X, et al. De novo mutations in childhood cases of sudden unexplained death that disrupt intracellular Ca(2+) regulation. *Proc Natl Acad Sci U S A*. Dec 28 2021;118(52)doi:10.1073/pnas.2115140118
23. Halvorsen M, Petrovski S, Shellhaas R, et al. Mosaic mutations in early-onset genetic diseases. *Genet Med*. Jul 2016;18(7):746-9. doi:10.1038/gim.2015.155
24. Friedman D, Chong D, Tarr A, Navis A, French J. Improving the Process of Seizure Classification and Diagnosis through DISCOVER: A Diagnostic Interview for Seizure Classification Outside of Video-EEG Recording. *Neurology*. 2013;80(7 Supplement):P03.123.
25. Bruni O, Ottaviano S, Guidetti V, et al. The Sleep Disturbance Scale for Children (SDSC). Construction and validation of an instrument to evaluate sleep disturbances in childhood and adolescence. *J Sleep Res*. Dec 1996;5(4):251-61. doi:10.1111/j.1365-2869.1996.00251.x
26. Berg AT, Shinnar S, Hauser WA, et al. A prospective study of recurrent febrile seizures. *N Engl J Med*. 1992;327(16):1122-7. doi:10.1056/nejm199210153271603
27. Vestergaard M, Pedersen MG, Ostergaard JR, Pedersen CB, Olsen J, Christensen J. Death in children with febrile seizures: a population-based cohort study. *Lancet*. Aug 9 2008;372(9637):457-63. doi:10.1016/S0140-6736(08)61198-8

Table 1. Characteristics of Respondents (N=381)			
	FS Only (n=328)	**FS+SUDC (n=53)**	***P***
Mother Survey Respondent	323/328 (98.5)	44/53 (83)	<.01
Referral Source			<.01
Social media	304/328 (92.7)	6/53 (11.3)	
Organization	17/328 (5.2)	45/53 (84.9)	
Doctor	1/328 (0.3)	0	
Other	6/328 (1.8)	2/53 (3.8)	
Education >16 years	193/320 (58.8)	34/53 (64.2)	0.53
Household Annual Income >70K	151/319 (46)	39/53 (73.6)	0.46

Table 2. Child Demographics (N=381)			
	FS Only (n=328)	**FS+SUDC (n=53)**	***P***
Male Sex	179/319 (54.6)	36/53 (67.9)	0.14
Race: White	259/317 (79)	40/52 (75.5)	0.53
Development Concerns	40/318 (12.2)	13/52 (24.5)	**0.03**
Mean Age at 1st Febrile Seizure in months, (SD) (% of cases with data)	19.0 (10.5), (325/328)	16.7 (5.13), (53/53)	**0.01**
Family History of Febrile Seizure	90/280 (27.4)	14/46 (26.4)	0.95
Family History of Epilepsy	17/303 (5.2)	3/51 (5.7)	1

Chi Square tests for Independence performed with Yates correction applied for 2x2 table. The "n" values calculated per number of responses for specific question. Student's T-test calculated to compare means of independent samples. F value used to compare homogeneity of variances and if significant, Welch test was used.

Table 3. Duration from Febrile Onset to Death and Age at Death in months (N=53)	
	FS+SUDC
Duration Febrile Onset to Death	
Mean (SD)	10.8 (9.82)
Median [Min, Max]	7.50 [0, 45.0]
Missing (%)	1 (1.9)
Age at Time of Death	
Mean (SD)	27.5 (10.2)
Median [Min, Max]	24.5 [15.0, 67.0]
Missing (%)	1 (1.9)

Table 4. Parasomnias Reported 6 Months Before and After 1st Febrile Seizure (N=381)			
	FS Only (n=328)	**FS+SUDC (n=53)**	***P***
Restless or Moved A lot in Sleep	92 (28.0)	7 (13.2)	
Missing	44 (13.4)	6 (11.3)	**0.02**
Awoke >2x/Night Never or Occasionally (≤1-2x/month)	122 (37.2)	33 (62.3)	
Missing	43 (13.1)	5 (9.4)	**0.001**
Talked in Sleep	28 (8.5)	2 (3.8)	0.35
Sleepwalked	3/283 (0.9)	1/46 (1.9)	1
Grinded Teeth	36/284 (11)	4/47 (7.5)	0.57
Awoke Screaming or with Nightmares	49/262 (14.9)	4/45 (7.5)	0.16

Table 5. Predictors of FS+SUDC vs FS Only: Adjusted Odd Ratios After Data Imputation of Missing Values (N=381)			
	aOR	**95% CI**	
Sex (Male)	1.04	0.42	2.62
First Degree Family History of Febrile Seizure	1.03	0.4	2.67
First Degree Family History of Epilepsy	1.65	0.33	8.29
Not Restless During Sleep	1.62	0.55	4.67
Awoke >2x/Night Never or Occasionally (≤1-2x/month)	**3.47**	**1.32**	**9.08**
Age at Febrile Seizure Onset (months)	0.96	0.91	1.01
Development Concerns	2.45	0.79	7.61
Time of day (ref=morning)			
Evening 5-10PM	1.12	0.44	2.87
Nighttime	0.19	0.02	1.61
Duration Not Respond (1min or more)	**0.34**	**0.14**	**0.85**
Drool	0.57	0.22	1.48

The adjusted ORs use multiple imputations (MICE package in R) to replace missing values using predictive mean matching based on 10 imputations to compute a logistic regression model to predict SUDC using all the covariates in the table. After the adjustments and imputations, there was still evidence of an association of the outcome with Never or occasionally waking twice and not responding for 1+ minutes.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: