



A Systematic Approach to Evaluate Sudden Unexplained Death in Children

Annelotte Maretta Pries, MD¹, Jopje Marlies Ruskamp, MD, PhD², Esther Edelenbos, MD³, Joris Fuijkschot, MD, PhD⁴, Ben Semmekrot, MD, PhD⁵, Krijn Teunis Verbruggen, MD, PhD⁶, Elise van de Putte, MD, PhD², and Patrycja Jolanta Puiman, MD, PhD¹

Objective To evaluate in the Netherlands the national outcomes in providing cause of and insights into sudden and unexplained child deaths among children via the Postmortem Evaluation of Sudden Unexplained Death in Youth (PESUDY) procedure.

Study design Children aged 0-18 years in the Netherlands who died suddenly were included in the PESUDY procedure if their death was unexplained and their parents gave consent. The PESUDY procedure consists of pediatric and forensic examination, biochemical, and microbiological tests; radiologic imaging; autopsy; and multidisciplinary discussion. Data on history, modifiable factors, previous symptoms, performed diagnostics, and cause of death were collected between October 2016 and December 2021.

Results In total, 212 cases (median age 11 months, 56% boys, 33% comorbidity) were included. Microbiological, toxicological, and metabolic testing was performed in 93%, 34%, and 32% of cases. In 95% a computed tomography scan or magnetic resonance imaging was done and in 62% an autopsy was performed. The cause of death was explained in 58% of cases and a plausible cause was identified in an additional 13%. Most children died from infectious diseases. Noninfectious cardiac causes were the second leading cause of death found. Modifiable factors were identified in 24% of non-sudden infant death syndrome/unclassified sudden infant death cases and mostly involved overlooked alarming symptoms.

Conclusions The PESUDY procedure is valuable and effective for determining the cause of death in children with sudden unexplained deaths and for providing answers to grieving parents and involved health care professionals. (*J Pediatr* 2024;264:113780).

In the Netherlands, an estimated 50 children (0-20 years) per year die from sudden unexplained deaths according to national death statistics.¹ Every unexpected child death is a tragedy, with a large impact on the family, community, and health practitioners involved. A thorough evaluation of the child's medical condition and the death circumstances may provide understanding of the cause of death to the families. Extensive evaluation of child deaths also provides a unique opportunity to identify diseases or potentially modifiable factors in professional and parental behavior that might be helpful for future prevention.

Evaluation of child deaths may be implemented in different ways. Many countries perform Child Death Reviews (CDRs), ie, multidisciplinary reviews of individual child deaths.²⁻⁶ In the United Kingdom, these have shown that a modifiable factor can be identified in up to 75% of cases of sudden, unexplained child deaths.^{7,8} Outcomes from CDRs have resulted in many public health recommendations in different countries such as Safe Sleep campaigns or better collaboration between health services.^{2,9,10} Another motive for investigating child deaths is to ascertain that no child maltreatment deaths remain undetected. The review by Milroy and Kepron¹¹ on the rate of covert homicide in sudden infant death syndrome (SIDS) estimates that 1%-10% of cases may be caused by maltreatment. Previous studies have called for a national diagnostic protocol for evaluating child deaths.^{12,13} However, to our knowledge, this has not yet happened outside of the Netherlands.

In the Netherlands, the evaluation of child deaths started in 1996 by systematically reviewing sudden unexpected deaths in infants cases <2 years of age. Following the CDR initiatives in the US, United Kingdom, Australia, and New Zealand, a pilot study was performed in 2011 implementing a CDR method in 2 Eastern provinces of the Netherlands modeled after the Child Death Overview Panel in the United Kingdom.² This pilot aimed to systematically overview all

From the ¹Department of General Paediatrics, Erasmus University Medical Center Sophia Children's Hospital, Rotterdam, The Netherlands; ²Department of Paediatrics, University Medical Center Utrecht Wilhelmina Children's Hospital, Utrecht, The Netherlands; ³Department of Paediatrics, Amsterdam University Medical Center Emma Children's Hospital, Amsterdam, The Netherlands; ⁴Department of Paediatrics, Radboud University Medical Center Amalia Children's Hospital, Nijmegen, The Netherlands; ⁵Department of Paediatrics, Canisius Wilhelmina Ziekenhuis, Nijmegen, The Netherlands; and ⁶Department of Paediatrics, University Medical Center Groningen Beatrix Children's Hospital, Groningen, The Netherlands

| | |
|--------|--|
| CDR | Child Death Review |
| PESUDY | Postmortem Evaluation of Sudden Unexplained Death in Youth |
| SIDS | Sudden infant death syndrome |
| USID | Unclassified sudden infant death |

0022-3476/© 2023 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).
<https://doi.org/10.1016/j.jpeds.2023.113780>

child deaths in children aged 29 days to 48 months. In 2 years, 6 of 18 cases were reviewed after parents gave informed consent. It was concluded that large-scale implementation of CDR was not possible in the Netherlands, due to lack of statutory basis and acceptance among professionals.¹⁴

The collaboration of Dutch health practitioners, legislators, and lawyers resulted in 2010 in a legal basis for a procedure reviewing unexplained child deaths. Law amendments obligated health practitioners to consult a forensic medical examiner before signing the death certificate of any deceased minor. Only the forensic medical examiner can determine a child's death to be natural or unnatural. In cases in which child death was to be expected, such as, for instance, children dying from severe, terminal illness either in the hospital or at home after palliative care, the forensic medical examiner will conclude a natural death based on the information provided by the reporting physician involved. In cases for which child death was unexpected, for example, in cases of trauma, suicide, or children collapsed without a known preceding severe disease, the forensic medical examiner determines the nature of the death by taking a history, gathering information from hospital patient files or other practitioners involved, performing a post-mortem physical examination, and looking for factors at the death scene that might raise suspicion of an unnatural cause of death. Deaths suspected to be unnatural are further mandatorily investigated by the Netherlands Forensic Institute.

In 2012, a pilot procedure was launched for children with an unexplained, natural death. The procedure was standardized, embedded in the law, and was meant to consist of a quick response containing an extensive history, physical examination, laboratory and radiologic examinations, information obtained from involved care providers, autopsy, and a multidisciplinary evaluation. The forensic medical examiner decided on and coordinated the procedure without parental consent, except for the autopsy. This procedure was performed in 2 university hospitals. The primary purpose was uncovering undiagnosed child abuse as a cause of death. The procedure did not uncover any child abuse, although it did show to be effective for identifying the cause of death.¹⁵ Evaluation by the Ministry of Justice and Security concluded that the procedure was too expensive and too demanding to be continued in the aforementioned form. In addition, since the pilot revealed no deaths by child maltreatment, it was concluded there was no legal ground to perform this procedure without parental consent.^{15,16}

Since the procedure did identify the cause of death in 70% of the completed cases, all involved health care professionals and parents were impressed with the high yield of causes of death.¹⁵ Subsequently, a modified procedure warranting parental consent was implemented nationally in 2016 and financed by the Ministry of Health, Welfare and Sport.¹⁷ This procedure is called the Postmortem Evaluation of Sudden Unexplained Death in Youth (PESUDY) procedure and is carried out in all 7 academic hospitals in the Netherlands.

The prospective study aimed to describe the outcomes of the PESUDY procedure and its diagnostic value. In addition, the presence of possible modifiable factors was investigated.

Methods

Study Sample

For this study, PESUDY cases between 2016 and 2021 were included if their parents or legal caregivers consented to at least 1 element of the procedure. Children (0-18 years) are eligible for the PESUDY procedure only if the forensic medical examiner deems their death unexpected and natural but without a clear cause of death (unexplained). A death is considered unexpected and unexplained when the child was previously presumed to be in good health, in stable chronic condition, or was experiencing acute illness not expected to cause death. No strict time definition is used. Examples of deaths that would be excluded from the procedure are deaths in terminal illnesses, clinical meningococemia, and all unnatural deaths. Cases of stillbirth or neonatal death in children never discharged home are also excluded from the procedure because for this group, a nationwide perinatal audit exists. The [Figure](#) shows the inclusion process for the PESUDY procedure.

PESUDY Procedure

The PESUDY procedure is funded by the Dutch Ministry of Health, Welfare and Sport. In case suspicions of child maltreatment do arise during the procedure, the procedure halts and the forensic medical examiner will discuss with the prosecutor for possible mandatory forensic examination at the Netherlands Forensic Institute. The PESUDY procedure consists of the following diagnostic elements:

- Postmortem physical examination performed by both the forensic medical examiner and pediatrician.
- Extensive, protocolled medical history taken by the pediatrician and abstraction of local medical records addressing items such as previous illnesses, recent symptoms, help-seeking behavior, timing, and circumstances of the death and the resuscitation attempt.
- Examination of the location at which the child became critically ill or died by the forensic medical examiner.
- Biochemical analysis including but not limited to blood (electrolytes, kidney function, liver function, cortisol, osmolality, creatine kinase, C-reactive protein, protein spectrum, complete blood count, and glucose) within 2 hours' postmortem, if possible, cerebrospinal fluid (cell count, protein, glucose), urinalysis, and vitreous humor (electrolytes).
- Microbiological analysis of cultures of blood, cerebrospinal fluid, urine, and sputum and respiratory panel polymerase chain reaction on sputum swab and *Bordetella pertussis* polymerase chain reaction on nasopharyngeal swab.
- Collection of additional materials such as feces, fibroblasts, and/or hair and storage for possible further analysis. If indicated by the pediatrician or the concluding multidisciplinary, audit materials including blood, urine, and spinal fluid were used for supplemental microbiologic, toxicologic, endocrinal, metabolic, or genetic investigations.

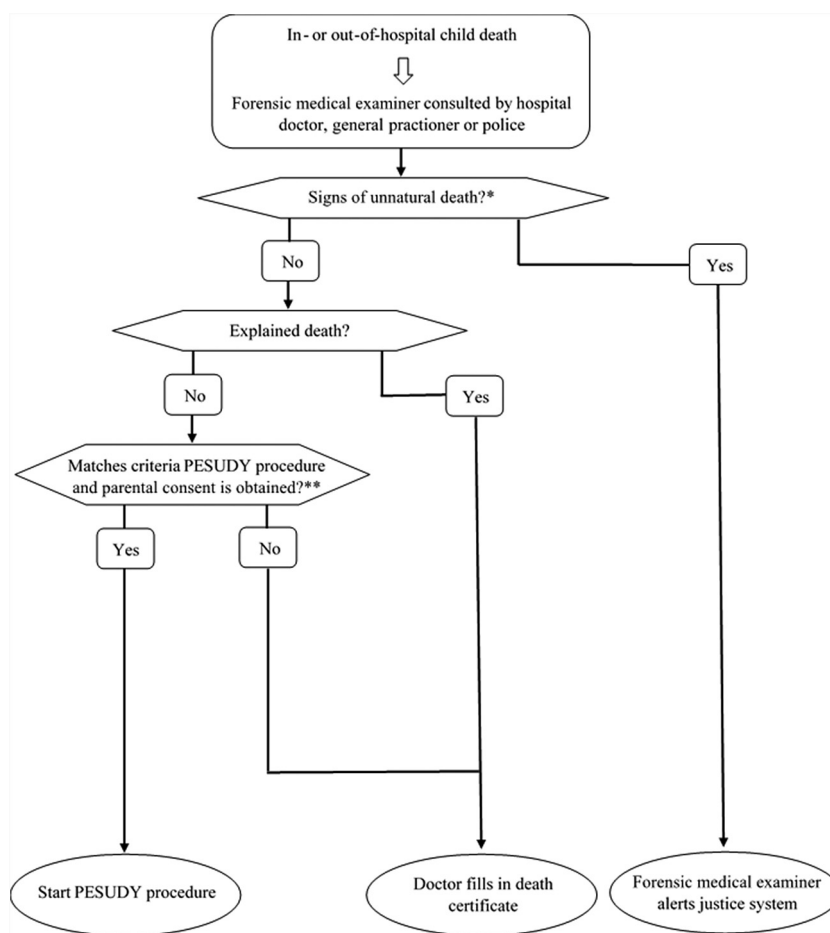


Figure. Selection of cases for PESUDY procedure.* The forensic medical examiner the death by taking a history, doing a postmortem physical examination, and looking for environmental factors. In some cases, the forensic medical examiner might delegate the gathering of this information to a doctor present at the location of the child.** If the death was a stillbirth or occurred in the perinatal period with the child having never left the hospital, a perinatal audit is preferred.

- Radiologic examination consisting of a skeletal survey in children <4 years and a computed tomography scan or magnetic resonance imaging scan of the entire body and if indicated funduscopy.
- Autopsy by a child pathologist and storage of tissue samples for possible further analysis.
- Collection of additional information from involved care providers such as the general practitioner, other hospitals, Preventive Child Healthcare, and Child Protection Services.

Conclusions on the cause of death and indication for supplemental investigations and screening of family members were made in a multidisciplinary audit with representatives from all specialties involved including but not limited to the general pediatricians, forensic medical examiners, radiologist, pathologist, geneticist, child cardiologist, child infectious disease specialist, metabolic disorder specialist, and SIDS expert. Parents were subsequently notified of the findings in a final meeting with the pediatrician who

performed the PESUDY procedure and asked for their feedback on the procedure, since the procedure also aims to properly guide the parents and other family members.

Definitions

Comorbidity was defined according to the Pediatric Medical Complexity Algorithm or prematurity and/or birth weight small for gestational age.¹⁸ The cause of death was determined in the multidisciplinary audit and could be categorized as explained, plausible, or unexplained. A cause was considered explained when postmortem findings corroborated with the history or the autopsy provided a full explanation. A cause was categorized as plausible when it was evidenced by a postmortem finding without a fitting history or vice versa. Lastly, a cause remained unexplained in the absence of a history or postmortem finding related to a lethal condition. For the unexplained cases in children <1 year of age, the per-exclusion diagnosis of SIDS was considered.

SIDS was defined according to the San Diego Definition: sudden unexpected death <1 year of age with the onset of the fatal episode occurring during sleep that remains unexplained after a thorough investigation including a complete autopsy, clinical history, and review of the circumstances of the death.¹⁹ The San Diego Definition also defines unclassified sudden infant death (USID) when a death meets the general criteria for SIDS but alternative diagnoses are equivocal, including cases for which autopsies were not performed.

Modifiable factors were identified for non-SIDS/USID cases according to the United Kingdom definition: factors that by intervention could potentially be modified to reduce the risk of future child deaths.² In other words, realistic moments in the case history where prevention of the death would have been possible. These factors could either involve professional care or care by caregivers and were identified and allocated into categories by consensus between 2 authors based on a qualitative review of the data.

Data Collection and Analysis

Detailed data of the medical history, postmortem physical examination, and diagnostic outcomes of the PESUDY procedure were documented in the local patient records. In a national database, anonymized patient data and process-oriented data were recorded using a standardized form with partly dichotomized items and open fields using Castor Electronic Data Capture. Data were collected from this database from the first PESUDY case in October 2016 until December 2021, spanning 63 months. Descriptive and statistical analyses of the quantitative data were performed using SPSS, Version 28.0 (IBM Corp. Released 2021. IBM SPSS Statistics for Windows).

Ethics

The Medical Research Ethics Committee of the University Medical Centre Utrecht (reference number WAG/mb/18/007175) exempted this study from review because the Medical Research Involving Human Subjects Act does not apply to deceased individuals.

Results

In total, 214 cases were investigated and in 212 cases consent was obtained for the use of data for research purposes. Most children collapsed in a home setting, namely 94%. In total, 64% of children were pronounced dead at home and 56% of all cases were male. The median age was 11.0 months (IQR, 3.0-72.5 months). In 33% of cases, the child had comorbidities. In 28%, professional care was sought before the child became critically ill.

The PESUDY procedure resulted in an explained cause of death in 58% (n = 123) of cases, which corresponds to 44% of cases <1 year and 72% of cases >1 year. In 13% (n = 27) a plausible cause was identified and in 29% (n = 62) the cause of death remained unexplained (Table I). Most children died from an infectious cause (n = 76 explained, n = 12 plausible).

In approximately one-half of these cases, the infection was located in a specific organ system, such as the cardiovascular (n = 21), respiratory (n = 14), or digestive system (n = 13) (Table II). In the children with an explained or plausible cause determined, the number of infectious causes was significantly greater for children <6 years old than in older children (*P*-value .004). Noninfectious cardiac, respiratory, or gastrointestinal causes were diagnosed in 19, 10, and 10 cases, respectively. Neurologic causes were found in 12 cases. Causes from other organ systems were rare. Of the 50 cases <1 year of age in which no cause of death was determined, 48 (22% of total cases) were given a SIDS or USID diagnosis. The other 2 remained undetermined.

Results from the different diagnostics performed in the PESUDY procedure are presented in Table III. In 196 (93%) cases, microbiological testing was performed. Toxicological and metabolic tests were performed in one-third of cases. Skeletal surveys (55%) were carried out mostly in children <1 year. In 95% of cases, either a computed tomography scan or magnetic resonance imaging was done. An autopsy was performed in 62% of cases, and almost one-half of these included autopsies of the brain. To look for differences in performed diagnostics between the PESUDY centers, the frequencies of used diagnostics were compared, and no large differences were found.

When comparing the number of performed diagnostics in explained, plausible and unexplained cases, the use of diagnostics was similar or greater in the cases with an unexplained cause of death in comparison with both explained and plausible causes (Table III). The certainties of causes of death per PESUDY center were determined and no significant differences between the centers were found.

In 4 cases, the cause of death was ultimately deemed unnatural because of foreign body asphyxiation or a traumatic cause of death. For a total of 6 cases, the PESUDY procedure was halted and transitioned into a full judicial forensic examination because of suspicious findings for abuse such as fractures or toxicological abnormalities. Further investigation by the Netherlands Forensic Institute did not lead to a conclusion of child abuse in these cases.

Modifiable factors were identified in 24% (n = 40) of non-SIDS/USID cases. Substandard professional care as a modifiable factor was identified in 30 cases. In most of these cases (n = 20) alarming symptoms such as difficulty breathing, neonatal fever and blue discoloration of the skin were overlooked or not handled according to guidelines. Other professional modifiable factors were insufficient instructions to parents (n = 3), failure of medical equipment (n = 1), and inadequate treatment or unrecognized treatment failure of a child admitted to medical-surgical units in hospitals (n = 6). Modifiable factors involving the care by caregivers were identified in 16 non-SIDS/USID cases and included leaving a sick child unsupervised for a long period of time (n = 1), not recognizing or acting on alarming symptoms

Table I. Number of cases with cause of death determined according to age group

| Age at death | Total cases n = 212 | Explained cause of death n = 123 | Plausible cause of death n = 27 | Unexplained cause of death n = 62 |
|--------------------|------------------------|-------------------------------------|------------------------------------|--------------------------------------|
| <1 year | 108 | 48 | 10 | 50 |
| Between 1 and 6 y | 55 | 40 | 7 | 8 |
| Between 6 and 12 y | 21 | 16 | 4 | 1 |
| ≥12 y | 28 | 19 | 6 | 3 |

(n = 13) and having dangerous items in the household in reach for the child (n = 1).

Final meetings for discussing the results of the PESUDY procedure with caregivers were held at a median time of 7.0 weeks following the death of the child. For 136 families, feedback on the PESUDY procedure was recorded in the patient records, and 135 of them were positive. Families reported being grateful for the support they received and being relieved to either know the cause of death or to know specific causes were ruled out.

Discussion

This study shows that the PESUDY procedure is a valuable and effective procedure for determining the cause of death in children with sudden unexplained deaths. The procedure resulted in an explained cause of death in 58% (n = 123) of cases, a plausible cause in 13% (n = 27), and 29% (n = 62) remained unexplained. Our data showed a large proportion of infections as the cause of sudden death. The PESUDY procedure also identified modifiable factors in 24% of cases. Families greatly appreciated the procedure.

We did not find any studies reporting on a national diagnostic protocol for sudden child deaths. Moreover, few studies report the frequency of postmortem diagnostics used in youth with sudden unexplained deaths. Fleming

et al describe the experiences of parents of children <4 years investigated by CDR in the United Kingdom.²⁰ In 69%, a pediatrician took a history and performed a postmortem physical examination. In the PESUDY procedure, the involvement of a pediatrician is standard. Fleming et al also reported a lower documented proportion of microbiological investigations (48%) and similar proportions of toxicological examinations.²⁰ In comparison to reports on postmortem investigations in sudden child deaths, the proportion of autopsies performed in the PESUDY procedure was 62% compared with 43%-92% found in the literature.^{4,5,12,13,21} Our autopsy numbers might be explained by the fact that autopsies for the PESUDY procedure were only performed in cases with full parental consent.

This highlights an important difference between previously reported international CDR procedures and the PESUDY procedure; namely the voluntary nature of the latter.^{2,6,22,23} In many countries and US states, CDR and/or autopsy is mandated in all child deaths to rule out child maltreatment.^{2,6,22,23} American reports on CDR investigating all child deaths showed 0.1%-2.0% died from previously unrecognized child maltreatment.^{24,25} A national survey on children's exposure to abuse in the US measured that 18.1% of 14- to 17-year-olds had been exposed to physical abuse in their lifetime.²⁶ A similar survey of professionals working with children in the Netherlands estimated the

Table II. Causes of death

| Type of cause | Explained n = 123 (% of cases) | | | | | Plausible n = 27 (% of cases) | | | | |
|------------------|-----------------------------------|---------|---------|--------|---------|----------------------------------|--------|--------|--------|---------|
| | Total | <1 y | 1-6 y | 6-12 y | ≥12 y | Total | <1 y | 1-6 y | 6-12 y | ≥12 y |
| Infectious* | 76 (62) | 30 (63) | 30 (75) | 7 (44) | 9 (47) | 12 (44) | 6 (60) | 4 (57) | 2 (50) | -(0) |
| General/sepsis | 31 | 16 | 11 | - | 4 | 7 | 4 | 2 | 1 | - |
| Cardiovascular | 20 | 2 | 10 | 5 | 3 | 1 | - | - | 1 | - |
| Respiratory | 12 | 7 | 4 | - | 1 | 2 | 1 | 1 | - | - |
| Gastrointestinal | 11 | 4 | 5 | 2 | - | 2 | 1 | 1 | - | - |
| Neurologic | 2 | 1 | - | - | 1 | - | - | - | - | - |
| Noninfectious† | 47 (38) | 18 (27) | 10 (25) | 9 (56) | 10 (53) | 15 (56) | 4 (40) | 3 (43) | 2 (50) | 6 (100) |
| Cardiovascular | 11 | 5 | 3 | 1 | 2 | 8 | 2 | 2 | - | 4 |
| Respiratory | 9 | 4 | 2 | 2 | 1 | 1 | 1 | - | - | - |
| Gastrointestinal | 10 | 4 | 3 | 3 | - | - | - | - | - | - |
| Nephrologic | 1 | - | - | 1 | - | - | - | - | - | - |
| Neurologic | 8 | 2 | 1 | 1 | 4 | 4 | - | 1 | 2 | 1 |
| Hematologic | 2 | 1 | 1 | - | - | - | - | - | - | - |
| Endocrinologic | 2 | - | - | 1 | 1 | - | - | - | - | - |
| Metabolic | 2 | 2 | - | - | - | 1 | - | - | - | 1 |
| Perinatal | - | - | - | - | - | 1 | 1 | - | - | - |
| Traumatic | 2 | - | - | - | 2 | - | - | - | - | - |

*Examples of infectious agents identified are group A streptococci, pneumococci, rotavirus, and influenza B virus.

†Examples of noninfectious causes are cardiomyopathies, volvulus, cerebral bleed, and pulmonary aspiration.

Table III. Performed diagnostics

| Diagnostics | Total cases n = 212 (%) | Explained cause of death n = 123 (%) | Plausible cause of death n = 27 (%) | Unexplained cause of death n = 62 (%) |
|-------------------------------|----------------------------|---|--|--|
| Microbiological | 196 (93) | 116 (94) | 26 (96) | 54 (87) |
| Toxicology* | 72 (34) | 33 (27) | 14 (52) | 25 (40) |
| Metabolic tests* | 68 (32) | 38 (31) | 7 (26) | 23 (37) |
| Endocrinal tests* | 41 (19) | 25 (20) | 5 (19) | 11 (18) |
| Skeletal survey under 1 y old | 116 (55) | 64 (52) | 11 (41) | 41 (66) |
| | 78 of 108 (72) | 37 of 48 (77) | 6 of 10 (60) | 35 of 50 (70) |
| CT scan | 96 (45) | 59 (48) | 11 (41) | 26 (42) |
| MRI scan | 153 (72) | 81 (66) | 21 (78) | 51 (82) |
| Autopsy total | 131 (62) | 83 (68) | 12 (44) | 36 (58) |
| Autopsy brain | 64 (30) | 39 (32) | 6 (22) | 19 (31) |

CT, computed tomography; MRI, magnetic resonance imaging.

*This testing was not part of the PESUDY protocol but performed by indication.

exposure to physical child abuse and neglect to be 1% of children.²⁷ Even though the PESUDY procedure is voluntary, in the Netherlands, all child deaths are judged by the forensic medical examiner. Unnatural in- or out-of-hospital deaths with medical or circumstantial signs suspicious for maltreatment are further mandatorily investigated by the Netherlands Forensic Institute. Because of this approach, and the fact that the previous pilot study showed no child abuse cases even though numbers were limited, voluntary CDR asking parents to consent to the different elements of the PESUDY procedure in unexpected child deaths without signs of trauma or any suspicion of maltreatment, is a feasible and preferable option in the Netherlands.¹⁵ Importantly, the PESUDY procedure can always be interrupted and transitioned into a full forensic examination when suspicion of child maltreatment arises during the procedure and the prosecutor imposes further investigation. Six cases in our study underwent such a forensic examination. No maltreatment was found.

The PESUDY procedure resulted in more successful identification of the cause of death and showed a greater number of infection-related deaths than previously described in reports on child death reviews for sudden death in youth.^{12,28} Bagnall et al, who included sudden unexpected death cases in children aged 1-15 years report that for 37% of children in their study a cause of death was determined.²⁸ Similarly, Burns et al report a cause of death based on the SDY Case registry in the US in 30% of cases <1 year and 59% of cases >1 year.¹² They describe mostly cardiovascular and pulmonary causes and only 3.6% were related to infection. An explanation for these differences could be the stricter definition of "sudden death" in these studies, defining it as either death within 1 or 24 hours after the onset of symptoms, which excludes children with infectious symptoms for a longer time. We, however, did include children with fever or mild infectious symptoms for >24 hours if death in these children still occurred unexpectedly and without explanation. We feel these children and their families also deserve a thorough work-up for a cause of death and want to seize the opportunity to learn more about inflammatory disorders, immunologic deficiencies, metabolic diseases, or even cardiovascular or pulmonary diseases aggravated by a normally "harmless" infection. Another possible reason for our greater

proportion of infectious causes is the routine microbiological testing that was performed in 93% of the PESUDY cases. We are not aware of studies on the frequency of microbiological testing for sudden death in youth in the US. However, in the United Kingdom percentages of 61% and 92% have been described.^{20,29}

The PESUDY procedure gave insight into the presence of modifiable factors showing a rate of 24% for all non-SIDS/USID cases. Identification of these factors provides valuable starting points for improvement of care. Previous studies investigating all child deaths report slightly lower rates of modifiable factors.^{5,7,8,24,25,30} Studies reporting on modifiable factors in all child deaths describe a percentage of preventable deaths of 26%-37%.^{5,7,8,25,30} These include deaths from external causes, which are likely to be preventable. When focusing on deaths by natural causes, the proportion of preventable deaths ranges from 3% to 20%.^{8,24,25,30} Our study focuses on sudden death cases, which we suspect are more prone to have modifiable factors at play. Interestingly, we found that 65% of modifiable factors were related to professional care and most involved failure to recognize severe illness in the child. This is in concordance with the results from Pearson et al, who report this as the most common factor as well and found that 64% of factors in all child deaths were related to health care.⁷

The PESUDY procedure holds several strengths and limitations. The first limitation is that no records are available to estimate the number of cases that would have been suitable for the PESUDY procedure but were not investigated because consent was not obtained. However, when we compared the estimated 50 children per year dying from sudden unexplained deaths in the Netherlands based on national death statistics with the average of 41 children per year included in the PESUDY procedure, the participation rate seems quite good.¹ A second limitation is the challenge posed by interpreting postmortem diagnostic results amid decomposition processes, especially since the autopsy rate was relatively low. As of writing this article, further investigations such as toxicological screening, metabolic testing, and genetic evaluation are not routinely performed in the PESUDY procedure, which might have led to missed diagnoses. However, in literature the toxicological screening and metabolic testing in

sudden unexplained death in youth are not reported to be performed routinely and according to limited studies, the diagnostic yield of routine screening is relatively low.^{31,32} An important strength of the PESUDY procedure is the standardization and documentation of the postmortem diagnostics used. We collected a large sample of cases from all over the Netherlands, providing the best possible representation of sudden unexplained deaths in children in our country. Therefore, this study provides a unique insight into sudden unexplained death in youth. This allows for a more differentiated interpretation of the proportion of cases in which the PESUDY procedure was able to identify a cause of death. The PESUDY procedure itself is a prime example of the advantages of a close collaboration between forensic examiners and pediatricians. We also sought parents' opinions on the PESUDY procedure and found they generally reported satisfaction and gratitude.

We believe being able to provide high-quality care to the families of a child with a sudden unexplained death is the main purpose of a CDR procedure. The PESUDY procedure yielded important results for both the caregivers and health practitioners involved. Future research into the PESUDY procedure may determine the relevance of specific postmortem diagnostics and elaborate on the experiences of those involved to improve the reviewing process. The next challenge for the PESUDY procedure will be to translate the modifiable factors identified into measures to improve the quality of care for children in general. ■

Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

We thank the PESUDY (in Dutch NODOK: Nader Onderzoek DoodsOorzaak bij Kinderen) collaborative for their support on this study: A. Custers (Department of Paediatrics, Maastricht University Medical Center, Maastricht, the Netherlands), E. Edelenbos (Department of Paediatrics, Amsterdam University Medical Center Emma Children's Hospital, Amsterdam, the Netherlands), J. Fuijkschot (Department of Paediatrics, Radboud University Medical Center Amalia Children's Hospital, Nijmegen, the Netherlands), B. Levelink (Department of Paediatrics, Maastricht University Medical Center, Maastricht, the Netherlands), E. van de Putte (Department of Paediatrics, University Medical Center Utrecht Wilhelmina Children's Hospital, Utrecht, the Netherlands), P. Puiman (Department of General Paediatrics, Erasmus University Medical Center Sophia Children's Hospital, Rotterdam, the Netherlands), J.M. Ruskamp (Department of Paediatrics, University Medical Center Utrecht Wilhelmina Children's Hospital, Utrecht, the Netherlands), B. Semmekrot (Department of Paediatrics, Canisius Wilhelmina Ziekenhuis, Nijmegen, the Netherlands), K.T. Verbruggen (Department of Paediatrics, University Medical Center Groningen Beatrix Children's Hospital, Groningen, the Netherlands), and H. Vlaardingbroek (Department of Paediatrics, Leiden University Medical Center, Leiden, the Netherlands).

Submitted for publication Jun 5, 2023; last revision received Oct 10, 2023; accepted Oct 11, 2023.

Reprint requests: Patrycja Jolanta Puiman, MD, PhD, Department of General Paediatrics, Erasmus Medical Center, dr. Molenwaterplein 40, 3015 GD, Rotterdam, The Netherlands. E-mail: p.puiman@erasmusmc.nl

References

1. Centraal Bureau Statistiek. CBS Statline Overledenen; doodsoorzaak (uitgebreide lijst), leeftijd, geslacht 2022. Accessed June 23, 2022. <https://opendata.cbs.nl/#/CBS/nl/dataset/7233/table?ts=1656511974367>
2. Fraser J, Sidebotham P, Frederick J, Covington T, Mitchell EA. Learning from child death review in the USA, England, Australia, and New Zealand. *Lancet* 2014;384:894-903.
3. Durfee M, Parra JM, Alexander R. Child fatality review teams. *Pediatr Clin North Am* 2009;56:379-87.
4. Mathews S, Martin LJ, Coetzee D, Scott C, Naidoo T, Brijmohun Y, et al. The South African child death review pilot: a multiagency approach to strengthen healthcare and protection for children. *S Afr Med J* 2016;106:895-9.
5. Numaguchi A, Mizoguchi F, Aoki Y, An B, Ishikura A, Ichikawa K, et al. Epidemiology of child mortality and challenges in child death review in Japan: the committee on Child Death Review: a committee Report. *Pediatr Int* 2022;64:e15068.
6. Vincent S. Child death review processes: a six-country comparison. *Child Abuse Rev* 2014;23:116-29.
7. Pearson GA, Ward-Platt M, Harnden A, Kelly D. Why children die: avoidable factors associated with child deaths. *Arch Dis Child* 2011;96:927-31.
8. Healthcare Quality Improvement Partnership. National Child Mortality Database. Child death review data: year ending 31 March 2021. NCMD programme; 2021. Accessed July 4, 2023. www.ncmd.info
9. Safeguarding and Vulnerable Children's Analysis Team. Child death reviews: year ending 31 March 2011. Official Statistics; 2011. Accessed July 4, 2023. <https://www.gov.uk/government/statistics/child-death-reviews-completed-in-england-year-ending-31-march-2011>
10. Douglas EM, Cunningham JM. Recommendations from child fatality review teams: results of a US nationwide exploratory study concerning maltreatment fatalities and social service delivery. *Child Abuse Rev* 2008;17:331-51.
11. Milroy CM, Kepron C. Ten percent of SIDS cases are murder—or are they? *Acad Forensic Pathol* 2017;7:163-70.
12. Burns KM, Bienemann L, Camperlengo L, Cottengim C, Covington TM, Dykstra H, et al. The sudden death in the young case registry: collaborating to understand and reduce mortality. *Pediatrics* 2017;139:e20162757.
13. Cottengim C, Parks S, Rhoda D, Andrew T, Nolte KB, Fudenberg J, et al. Protocols, practices, and needs for investigating sudden unexpected infant deaths. *Forensic Sci Med Pathol* 2020;16:91-8.
14. Gijzen S, Hilhorst MI, L'Hoir MP, Boere-Boonekamp MM, Need A. Implementation of child death review in The Netherlands: results of a pilot study. *BMC Health Serv Res* 2016;16:235.
15. Edelenbos E, Das K. Overleden kinderen: stand van zaken rond meldingsplicht en NODO1-procedure. *Bijblijven* 2014;30:41-8.
16. van Rijn MJ. Vaststelling van de begrotingsstaten van het Ministerie van Volksgezondheid, Welzijn en Sport (XVI) voor het jaar 2014 nr. 80. In: Ministerie van Volksgezondheid Welzijn en Sport. Den Haag: Tweede Kamer der Staten-Generaal; 2014.
17. Schippers EI. Vaststelling begroting Ministerie van Volksgezondheid, Welzijn en Sport (XVI) voor het jaar 2016 nr. 164. In: Ministerie van Volksgezondheid Welzijn en Sport. Den Haag: Tweede Kamer der Staten-Generaal; 2016.
18. Simon TD, Cawthon ML, Stanford S, Popalisky J, Lyons D, Woodcox P, et al. Pediatric medical complexity algorithm: a new method to stratify children by medical complexity. *Pediatrics* 2014;133:e1647-54.
19. Krous HF, Beckwith JB, Byard RW, Rognum TO, Bajanowski T, Corey T, et al. Sudden infant death syndrome and unclassified sudden infant deaths: a definitional and diagnostic approach. *Pediatrics* 2004;114:234-8.
20. Fleming P, Pease A, Ingram J, Sidebotham P, Cohen MC, Coombs RC, et al. Quality of investigations into unexpected deaths of infants and young children in England after implementation of national child death review procedures in 2008: a retrospective assessment. *Arch Dis Child* 2020;105:270-5.

21. Yurkovich C, Nazer D, Farooqi A, Kannikeswaran N. Does postmortem imaging provide additional findings after unexpected deaths in infants and children? *Pediatr Emerg Care* 2022;38:e1118-22.
22. Fraser J, Sleaf V, Sidebotham P. National child death review statutory and operational guidance: key concepts for practising paediatricians. *Arch Dis Child Educ Pract Ed* 2020;105:244-50.
23. Quinton RA. Child death review: past, present, and future. *Acad Forensic Pathol* 2017;7:527-35.
24. Rimsza ME, Schackner RA, Bowen KA, Marshall W. Can child deaths be prevented? The Arizona Child Fatality Review Program experience. *Pediatrics* 2002;110:e11.
25. Luallen JJ, Rochat RW, Smith SM, O'Neil J, Rogers MY, Bolen JC. Child fatality review in Georgia: a young system demonstrates its potential for identifying preventable childhood deaths. *South Med J* 1998;91:414-9.
26. Finkelhor D, Turner HA, Shattuck A, Hamby SL. Prevalence of childhood exposure to violence, crime, and abuse: results from the national survey of children's exposure to violence. *JAMA Pediatr* 2015;169:746-54.
27. Alink LPM, van Berkel S, Linting M, Klein Velderman M, Pannebakker F. NPM 2017: Nationale Prevalentiestudie Mishandeling van Kinderen en Jeugdigen. Leiden: Universiteit Leiden/TNO; 2018.
28. Bagnall RD, Weintraub RG, Ingles J, Duflou J, Yeates L, Lam L, et al. A prospective study of sudden cardiac death among children and young adults. *N Engl J Med* 2016;374:2441-52.
29. Pryce JW, Roberts SEA, Weber MA, Klein NJ, Ashworth MT, Sebire NJ. Microbiological findings in sudden unexpected death in infancy: comparison of immediate postmortem sampling in casualty departments and at autopsy. *J Clin Pathol* 2011;64:421-5.
30. Onwuachi-Saunders C, Forjuoh SN, West P, Brooks C. Child death reviews: a gold mine for injury prevention and control. *Inj Prev* 1999;5:276-9.
31. Langlois NE, Ellis PS, Little D, Hulewicz B. Toxicologic analysis in cases of possible sudden infant death syndrome: a worthwhile exercise? *Am J Forensic Med Pathol* 2002;23:162-6.
32. Matshes EW, Hamilton LE, Lew EO. Routine metabolic testing is not warranted in unexpected infant death investigations. *Acad Forensic Pathol* 2012;2:346-56.