British Journal of Medicine & Medical Research
3(1): 80-93, 2013

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The Sudden Infant Death Syndrome is a Probability Process

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Authors' contributions

This work was carried out in collaboration between all authors. Author DTM prepared the analyses of the 4-parameter lognormal distribution and prepared the first draft. Author EMD prepared the genetic analyses and jointly revised the draft with author DTM. All authors read and approved the final manuscript.

Research Article

Received 7th August 2012
Accepted 7th November 2012
Published 8th December 2012

ABSTRACT

The Sudden Infant Death Syndrome (SIDS) is sudden-unexpected death of an infant that remains unexplained after thorough forensic autopsy, death scene investigation and review of the infant's medical history. As the results of a few spins of a roulette wheel cannot establish whether the wheel is honest (uniform value distribution), medical investigations of a few SIDS cases have not been able to uncover the mechanistic cause of death. We propose that this is because statistical analyses of large numbers of independent observations may be required to unmask the apparent probability processes that govern these quite different phenomena. The SIDS male fraction ~0.60 appears as a binomial probability sample characteristic of a condition caused by an X-linked gene. The unique SIDS age distribution (minimum at birth, mode ~63 days, median ~94 days, falling exponentially to zero at ~41.2 months) appears as a probability sample from an underlying Johnson S_B (4-parameter lognormal) distribution of ages. The presence of this lognormal distribution is *prima facie* evidence that a probability process is involved. Matching binomial and S_B distribution equations to these physiological phenomena, we propose: The SIDS binomial gender distributions arises from an X-linked recessive allele ($q \approx 2/3$) non-protective against acute anoxic encephalopathy; and SIDS Johnson S_B age distributions arise from such genetically susceptible infants having

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three independent risk factors: neurological prematurity $(m + 0.31)^{-1}$ decreasing with age in months m; risk of respiratory infection increasing with age $(41.2 - m)^{-1}$; and risk of physiological anemia rising and falling with age $(2\pi\sigma^2)^{-1/2}[\exp(-0.5[(y-\mu)/\sigma]^2)]$, where $y = \text{Log}[(m + 0.31)/(41.2 - m)] = \mu + \sigma z$, μ is median of y, σ is standard deviation of y, with z a standard normal deviate. We show infant Respiratory Distress Syndrome and Suffocation by Inhalation of Food or Foreign Object have approximately the same male fractions as SIDS, supporting the hypothesis that the same allele of an X-linked gene is responsible for death in all these cases.

Keywords: SIDS; binomial distribution; 4-parameter lognormal distribution; respiratory distress syndrome; X-linkage.

DEFINITIONS AND ACRONYMS

CDC: U.S. Centers for Disease Control and Prevention; ICD: WHO International Classification of Diseases; OMB: U.S. Office of Management and Budget; RDS: Respiratory Distress Syndrome, also known as Hyaline Membrane Disease; SIDS: Sudden Infant Death Syndrome; SIFFO: Suffocation by Inhalation of Food, Gastric Content or other Foreign Object; SRD: Sudden Respiratory Deaths. All respiratory deaths that was unexpected or unattended, thereby mandating an autopsy. Includes pulmonary infections, allergy associated with respiratory system, pneumonia of the newborn, sudden death (cause unknown) and accidental mechanical suffocation and inhalation.

1. BACKGROUND/INTRODUCTION

The cause of the Sudden Infant Death Syndrome (SIDS) remains as possibly the biggest mystery in medicine [1, 2]. SIDS almost always occurs suddenly and silently for a sleeping infant, usually under 1-year of age [3] for which the parents or care-givers had no warning that the infant was at imminent risk of death. A thorough forensic autopsy is then performed, the death scene is investigated by the authorities, and the infant's medical history record is carefully examined. Yet, in spite of such sharply focused investigations by forensic experts and medical detectives, and identification of the non-causal risk factors present, no definitive cause of the death is found. This results in terrible psychological trauma for the parents who suffer the burden of their unexpected and unexplained loss. The following work may relieve their anxiety as we suggest that the child's death by SIDS was a random possibly-unpreventable physiological phenomenon.

We propose that rather than looking at single cases for evidence of the possible cause of SIDS, one needs to stand back and look at the statistical properties of a large ensemble of SIDS cases to see the classical epidemiologic patterns that emerge which provide the clues for solving this mystery. This is the same situation as where a single flip of a coin cannot reveal whether the coin is honest (P heads = 1/2) or the single spin of a roulette wheel cannot reveal whether the wheel is honest (generates a uniform distribution of 37 possible values as 0, 1, 2, …, 36). A large number of realizations are required so that a thorough statistical analysis can be performed with confidence to evaluate the likelihood that the coin or wheel is honest. However, many researchers on SIDS have relied on studies of small numbers of cases resulting in claims about SIDS that cannot be sustained with larger samples. For example, it was suggested that SIDS may have a 100% male excess based on a small sample of Finnish SIDS [4], where large samples of U.S. SIDS show the male

excess is 50% [5]. We develop here the position that analyses of the statistical properties of sufficiently large numbers of SIDS cases are required to provide the necessary clues for uncovering the statistical and physiological bases of SIDS.

In all the medical literature there is no hypothesis, other than an X-linkage, that can explain the consistent male excess of ~50% (male fraction ~0.60) that is observed in these cases because the other possible causes of male excess mortality from androgen interactions and male hyperactivity do not apply to SIDS [6-8]. Although some authors look at autosomal genes as possibly being associated with SIDS, they do not account for the fact that they are possessed with equal frequencies by males and females, so they cannot cause the constant male excess. For example, Paterson et al. [9] studied a small sample of SIDS (n = 16) and found a possibly autosomal-related serotonin deficiency greater in males than females that disappeared, as expected, when the authors studied a larger sample size of SIDS ("In this data set we found no effect for male sex") [10]. All accepted SIDS risk factors, such as prone sleeping position, low maternal age and education, parental tobacco smoking, and neurological prematurity are all independent of infant gender. However, we found that the male excess is similarly of order 50% in virtually all fatal respiratory conditions [11].

In this case the consistent excess XY male fraction of ~0.60 leads to the hypothesis of an extra XX female protection against SIDS provided by their second X-chromosome. The XY male with only one X chromosome receiving a recessive X-linked allele has no possibility of receiving the benefit of its complimentary dominant X-linked allele. We also present gender data on Respiratory Distress Syndrome (RDS), Suffocation by Inhalation of Food or Foreign Object (SIFFO) and autopsied unexpected Sudden Respiratory Death (SRD) with the same male fraction as SIDS and similar age distribution for SRD as SIDS supporting the possibility that the terminal mechanisms for SIDS, RDS, SIFFO and SRD are the same.

SIDS has multiple known risk factors that should not be confused with a pathological cause of death. Identical twins have virtually identical risk factors but they rarely die of SIDS simultaneously. The prone sleeping position is now known to be associated with a higher risk for SIDS than the supine sleep position [12], suggesting that rebreathing exhalations with higher CO_2 and lower O_2 may be involved. Increasing maternal age and increasing years of maternal education are both associated with decreasing risks of SIDS, perhaps associated with better maternal skills and knowledge. This may allow these older and more educated mothers to sooner recognize symptoms of respiratory infection requiring medical attention and to act on them promptly [13]. It is interesting to note that SIDS has a seasonality, matching that of respiratory infection with 20% more SIDS in January than in July for the U.S. from 1999-2009, that has not changed with the change in sleeping position [3] but the American Academy of Pediatrics Task Force on SIDS, perhaps from looking at smaller data sets, incorrectly claimed "it is no longer apparent [14]." Carpenter and Gardner [15] reported on the lognormal ages and genders (0.605 male) of all unexpected Sudden Respiratory Deaths (SRD) requiring autopsy in England and Wales from 1965 to 1976. SRD covered all respiratory infectious diseases, respiratory conditions such as suffocation and inhalation of food, and SIDS. We found that they had approximately the same male fraction and age distribution as modern SIDS leading us to propose that these deaths are all from the same mechanistic event, reached by different physiological paths [16].

Finally we note that the presence of the 4-parameter lognormal distributions of SIDS and SRD ages is *prima facie* evidence that they are resulting from a probability process. This is because both the normal and lognormal distributions can be derived from the mathematical

theory of probability that results when a number of unrelated, continuous random variables are added or multiplied together, respectively [17].

2. MATERIALS AND METHODS

For evaluating the binomial distribution of SIDS genders by race we utilize vital statistics that are publically available at the U.S. Centers for Disease Control and Prevention (CDC) web site [3]. These 42-years of U.S. SIDS data are coded by International Classification of Diseases (8ICD 795, 1968-1978; 9ICD 798.0, 1979-1998; 10ICD R95, 1999-2009). For comparison we also analyze similar mortality data on Infant Respiratory Distress Syndrome (RDS: 8ICD 796, 1968-1978; 9ICD 476, 1979-1998; 10ICD P22, 1999-2009) and children's Suffocation from Inhalation of Food or Foreign Object (SIFFO: 8ICD 911-912, 1968-1978; 9ICD 911-912, 1979-1998; 10ICD W78-W80, 1999-2009) [3]. For evaluating the detailed monthly age distribution of SIDS cases and plotting procedures, we rely on published age data, and personal communications from several of those authors that we tabulated previously [16]. Because SIDS occurring at ages over 1-year are not reported as SIDS, we estimated the numbers of unreported SIDS between 1 year and 41.2 months by semi-log extrapolation of the numbers of monthly SIDS between 4 and 12 months out to 41.2 months [18, 19].

As opposed to classical statistical analyses where individual realizations of a random process are assumed to be reported without error (i.e., heads or tails of a coin flip, the number on which a roulette ball lands, or the gender of a decedent) vital statistics related to race, age, and cause of death of an infant have experimental and reporting errors associated with them that are expected to inflate the variance of the data and invalidate the strict interpretation of statistical tests based on assumptions that 'sampling error' is the only source of variance. We therefore propose that the visual presentation of the linearity of these age data supports the model fit [16].

2.1 Errors in Diagnoses

SIDS is a diagnosis of exclusion and "Pathologists welcomed the diagnosis: the less they found, the more certain they could be [20]." Given the variability in the experience and expertise of the pathologists, differences in opinions can exist when viewing the same results [21]. In sinister circumstances, false positive SIDS can occur from infanticide by gentle suffocation with a soft pillow that leaves no trace [13]. False negative SIDS can occur if a non-lethal congenital anomaly or low-grade respiratory infection is mistakenly given as cause of death [21].

2.2 Errors in Age

Ages of SIDS are normally reported as occurring in a given month of life attained. However, a month is of indeterminate length (28-31 days). Given that 4-years constitutes (1 + 4 x 365) days and 48 'months', then intervals of 30.44 days/month should be the basis of reporting ages as months of life attained with statistical uniformity of the intervals analyzed. Table 1 shows examples of the age errors that can be created by different conventions for reporting monthly SIDS data [16]. These errors contribute to the variability of the statistical models fit to these data and complicate the interpretation of differences between predicted and observed values of numbers of deaths per month.

Table 1. Examples of different definitions of days to reach a full month of life completed as used by U.S. Centers for Disease Control and Prevention (CDC) and Australian Bureau of Statistics (ABS) compared to exact number of days with correction for leap year [16]

Month	1	2	3	4	5	6	7	8	9	10	11	12
Exact	30.44	60.88	91.31	127.75	152.19	182.63	213.06	243.50	273.94	304.38	334.82	365.25
CDC[a]	28	63	91	126	154	182	210	245	273	301	336	364
ABS[b]	31	60	90	120	150	180	210	240	270	300	330	360

[a]*personal communication: weeks converted to months, Kimberley D. Peters, U.S. CDC, February 2, 1998.*
[b]*personal communication: days converted to months, Louise Ellis, SIDS and Kids, Australia, October 5, 2010.*

2.3 Errors in Race

The race of an infant at birth is usually reported either as the race of the mother or as identified by her. Whereas this presents no problem when both parents are of the same race (White/White or Black/Black) there are often complications when the father is unknown, or parents are of different races (Black/White) or are of mixed race themselves (e.g., Black-White/White or Black-White/Black). "In the 1980 and 1990 censuses, for example, race was reported as "Black" for two-thirds of children in families with one 'Black' parent and one 'White' parent present [22]." In this paper such arbitrary assignment of a single race creates genetic errors and is expected to inflate the variance of the statistics of the racial data. Given that a biracial infant's Black and White parents are XY male and XX female, an XY male infant will receive his X chromosome from his mother so it makes a difference if his mother is Black or White. Suffice it to say that biracial or multiracial parents complicate a genetic analysis beyond the scope of this paper.

3. RESULTS AND DISCUSSION

3.1 The Binomial Distribution of Gender in SIDS and Other Respiratory Causes of Infant Death

3.1.1 SIDS

The gender distribution of U.S. SIDS cases shows an approximate ~50% male excess that has not changed during the past 42 years during which the rate of SIDS has decreased by ~50% related to the discovery that the prone sleep position is a major risk factor for SIDS. For example, a 'back-to-sleep' campaign has reduced the rate of U.S. SIDS from ~5,000 per year in 1979 to ~2,200 per year in 2009 but did not change the male fraction. Table 2 shows the total numbers of U.S. SIDS by race/ethnicity and gender for the 42-year period 1968 to 2009 [3]. The CDC [3] only reports racial data for Black, White and Other-races-combined from 1968-1998 so those categories are also used for 1999-2009.

These deaths shown in Table 2 occur by different causes, such as accident (SIFFO), disease (RDS) and unknown with risk factor influences (SIDS). However, they have the same approximate male fraction in large numbers of cases. This led us to hypothesize [16, 23] that the terminal event in all these respiratory conditions is caused by the same gender-related mechanism. Given the intense investigations of SIDS deaths by pathologists and others, SIDS must have a common terminal event with other sudden unexpected respiratory deaths that is not investigated at autopsy, such as cerebral anoxia caused by an X-linkage.

Table 2. Summary of deaths from SIDS, Respiratory Distress Syndrome (RDS), and Suffocation by Inhalation of Food or Foreign Object (SIFFO) in the U.S. 1968-2009 by race and gender. Male fraction of SIDS and RDS are for males and females < 1 year. SIFFO data are for all U.S. children < 10 years to increase sample size [3]

Cause of death 1968-2009	Race[a]	ICD codes	Male cases, M	Female cases, F	Male fraction of deaths, M/(M+F)
SIDS	White	8ICD 795; 9ICD 798.0; 10ICD R95	60,165	37,550	0.6157
SIDS	Black	8ICD 795; 9ICD 798.0; 10ICD R95	24,815	19,066	0.5655
SIDS	Other	8ICD 795; 9ICD 798.0; 10ICD R95	2,929	2,066	0.5864
RDS	White	8ICD 776; 9ICD 769; 10ICD P22.0	72,434	43,698	0.6237
RDS	Black	8ICD 776; 9ICD 769; 10ICD P22.0	22,936	16,145	0.5869
RDS	Other	8ICD 776; 9ICD 769; 10ICD P22.0	1,673	997	0.6266
SIFFO <10 years	White	8ICD 911, 912; 9ICD 911, 912; 10ICD W78-80	3,785	2,518	0.6005
SIFFO <10 years	Black	8ICD 911, 912; 9ICD 911, 912; 10ICD W78-80	1,514	1,208	0.5562
SIFFO <10 years	Other	8ICD 911, 912; 9ICD 911, 912; 10ICD W78-80	260	162	0.6161

[a]*A single race assigned to some cases may cause an error due to multiracial parentage (OMB, 1995).*

An uninvestigated physiological characteristic of SIDS may be an X-linked gene locus, presently unidentified, that has two alleles: A recessive allele, non-protective of SIDS, occurring with a racially dependent frequency of order q = 2/3; and a dominant allele, protective of SIDS, occurring with a frequency of order $p = 1 - q = 1/3$ [5, 23]. This protection is proposed to arise from the dominant allele coding for an enzyme that allows the subject to shift from aerobic oxidation to anaerobic oxidation in respiratory control neurons during a transient period of potentially-lethal acute anoxic encephalopathy. An XY male infant would be at risk of possessing the recessive allele with probability q = 2/3. An XX female infant would be at risk of possessing only the recessive allele with probability of $q^2 = (2/3)(2/3) = 4/9$. The ratio of 2/3 to 4/9 is 1.5:1 corresponding to a ~50% male excess risk and a male fraction of ~0.60 for equal numbers of males and females born during the year who are at risk. Another risk factor for SIDS that is not measured at autopsy is the extent of infant physiological anemia [24], but this may affect the age distribution, not the gender distribution. See discussion below of the 4-parameter lognormal age distribution [18, 19, 25].

We call attention to the remarkable consistency in Table 2 of the male fractions for White SIDS, RDS and SIFFO data. These values respectively are 0.6157, 0.6237, and 0.6005, respectively. For an exact calculation of the recessive allele fraction of order q = 2/3, we use the relation of the male fraction x to q as shown in Equation 1, with a correction for the White 5% male birth excess:

$$x = 1.05\,q / (1.05\,q + q^2) = 1/(1 + q/1.05) \text{ and } 1 + q/1.05 = 1/x \quad (1)$$

For SIDS, $x = 0.6157$ and $1/0.6157 = 1.6242$, so $q = (1.05)\,0.6242 = 0.6554$

Each death by these causes is independent of all others and consequently these data represent independent and random realizations of large numbers of cases (~98,000 SIDS, ~116,000 RDS, and ~6,000 SIFFO). The male fraction data for the Black infant SIDS, RDS and SIFFO are 0.5655, 0.5869, and 0.5562 respectively but with smaller numbers of cases. Because of the artifact of CDC giving only a single race for an infant when the parents are biracial or multiracial and the propensity to list such an infant as Black when one of the parents is Black, we propose that this larger male fraction variability amongst the 'Black' respiratory cases may be due to the larger presence of White-ancestral genes with different allele frequencies in their genomes than Black ancestral genes in the White cohort [22]. For all other races combined, the male fraction of SIDS is 0.5864, well within the range of the Black and White male fractions.

3.1.2 Respiratory distress syndrome (RDS)

RDS is also known as idiopathic hyaline membrane disease. Infants born with RDS are cyanotic at birth and their diagnoses are rapid and treatment is promptly initiated. Because the RDS disease is obvious at birth and the infants are under treatment, autopsy of RDS cases is not mandated and consequently is infrequent. Therefore, some RDS infants may die from congenital anomalies or other hidden causes that are undiagnosed. The genes responsible for their defective pulmonary surfactant process are autosomal and for equal numbers of males and females born, equal numbers of males and female infants are at risk of RDS. Although recent advances in treatment have reduced RDS deaths in the U.S. from ~4,500 in 1979 to ~700 in 2009 [3], the White male fraction has remained the same and is virtually identical for that of White SIDS (0.6237 RDS and 0.6157 SIDS) as shown in Table 2. Black RDS male fraction is 0.5869 which is higher than the Black SIDS male fraction of 0.5655, perhaps because of the smaller sample size and rarity of RDS autopsy [3].

3.1.3 Suffocation from inhalation of food or foreign object (SIFFO)

The risk of SIFFO for an infant or young child at any age is independent of gender. Virtually all such cases are autopsied (the item inhaled is identified as food, foreign object or gastric content). Table 2 shows the total numbers of SIFFO for infants and young children from birth to age < 10-years (to increase N), well below the ages when young males begin to drink alcohol more than females of same age. Because the male fraction is constant for this cause of death from birth through 10 years, the mechanism causing the 50% male excess cannot be related to an infant's physiological development. The ~6,000 White SIFFO cases have a male fraction of 0.6005 (lower than those for White SIDS and RDS) and ~3,000 Black SIFFO cases have a male fraction of 0.5562 (similar to that for Black SIDS).

The food-related risk factors for SIFFO are found in the type and preparation of food that in the U.S. is the same for male and female infants and children. Common items found at autopsy are balloons, grapes, nuts, hot dog slices, small coins, etc. [26]. These cases are all independent of each other and there is no reason found in the literature why males should be more at risk of dying from SIFFO than females. We propose that equal numbers of males and females inhale such items per equal numbers of similar race and age at risk. Emergency medical care is given almost immediately to the victims independent of race or gender, but ~50% more males than females die from choking on the inhaled items. We propose that

those who cannot be saved by emergency medical care are the ones with only the hypothesized X-linked recessive allele that is not protective of cerebral anoxia. Those with a dominant protective allele would have temporary protection against an anoxic death of respiratory control neurons in their brainstem (acute anoxic encephalopathy) if emergency aid is promptly applied [18, 22].

3.1.4 Comparison of SIDS with RDS and SIFFO

It should be noted that SIDS is quite different in practice than RDS and SIFFO. Death is the first symptom of SIDS and consequently the number of males and females with first symptoms are the numbers that die. This is in contrast to RDS and SIFFO where the first symptoms are cyanosis and choking, respectively. This allows medical treatment to be given to those with SRD and emergency treatment to those with SIFFO thereby saving the lives of some of these infants. In mathematical terms let male SIDS be Msids and female SIDS be Fsids. The male fraction of SIDS is then

$$xSIDS = Msids/(Msids + Fsids). \quad (2)$$

However, for RDS (and similarly for SIFFO), Mrds = Mrds(at risk) - Mrds(saved) and Frds = Frds(at risk) - Frds(saved). Therefore the male fraction of RDS, xRDS is

$$xRDS=[Mrds(at\ risk)-Mrds(saved)]\ /[Mrds(at\ risk)-Mrds(saved)+Frds(at\ risk)-Frds(saved)] \quad (3)$$

The subtraction of the numbers of saved male and female cases increases the variance of the resulting reported male fraction of deaths and contribute to their differences from the male fraction of SIDS.

3.2 The 4-Parameter Lognormal Age Distribution of SIDS and other Infant Sudden Respiratory Deaths (SRD)

Table 3 shows the age distribution of Sudden Respiratory Deaths (SRD) in infancy as the number of cases occurring in the first 12 months of life attained. These SRD are defined as an unexpected infant death from a respiratory cause requiring autopsy, of which approximately 70% are SIDS, with a male fraction of 0.605 [14, 27]. These data are combined from 11 studies [16] which used different definitions of a month of life as previously discussed. A left-censored Johnson S_B distribution (4-parameter lognormal) is fit to these data and models SIDS and SRD as a bounded variable between a minimum age at birth (m = 0) and a maximum age (m = 41.2 months) [16, 18,19]. Equation 4 is the probability density function of this distribution where monthly age m, bounded between ages a and b, is transformed into a variable y that is normally distributed between -∞ and +∞ where y = Log [(m - a)/ (b - m)]. μ is the median of y, σ is its standard deviation, and a and b are the third and fourth parameters respectively.

$$dp(m)/dm = (2\pi\sigma^2)^{-1/2}\ [(m - a)^{-1} + (b - m)^{-1}]\ \exp(-0.5[(y - \mu)/\sigma]^2);\ a < m < b \quad (4)$$

where $y = \mu + \sigma z$, with z a standard normal deviate. Note that in the limit as a goes to zero and b goes to +∞, equation 4 becomes the classical 2-parameter lognormal distribution.

Fig. 1 is a log-probability plot of the transformed variable y = Log [(m + 0.31)/ (41.2 - m)] versus the standard normal deviate z converted to percentage. We used the values of

a = -0.31 months and *b* = 41.2 months previously developed by maximum likelihood [17], and the median μ and slope σ are found to be -1.03 and 0.31, respectively. The equation is censored at *m* = 0 and the number of SIDS and SRD predicted with ages less than or equal to zero are all taken to occur at birth where *m* = 0. The patent linearity of these monthly values of y and *z* is taken as evidence of the goodness of fit of the model to these data, as the experimental errors in age and diagnoses described above make the standard statistical tests inaccurate.

Equation 4 can be interpreted as the product of three independent age-dependent risk factors corresponding to the probability that they will all coincide at the same age, *m* [17]: The first risk decreases with age as p1 = 1/(*m* - *a*); The second risk increases with age as p2 = 1/(*b* - *m*); the third risk factor is normally distributed, rising with age from zero to a maximum and falling to zero as p3 = $(2\pi\sigma^2)^{-1/2}$ exp(-0.5[(y - μ)/σ]^2). Note that [1/(*m* - *a*) + 1/(*b* - *m*)] can also be written as (*b*-*a*)/ [(*m*-*a*) (*b*-*m*)]. Examining the SIDS risk factors in the literature we match the first risk factor to neurological prematurity that decreases with age [15]; the second risk factor is matched to risk of respiratory infection that increases as the infant gets older and has more contact with others outside the home [13]; the third risk factor is that of having a natural physiological anemia that occurs in infancy [24]. The infant's blood hemoglobin is maximal at birth from placental transfusion, and decreases to a nadir at 2-3 months when fetal hemoglobin disappears faster than it can be replaced by adult hemoglobin, followed by a slow increase as adult hemoglobin takes over.

An infant's anemia cannot be evaluated at the SIDS autopsy as total hemoglobin can only be measured accurately in living infants because of hemolysis and lividity [24] which may be a contributing reason why SIDS has gone so long without an explanation.

It should be noted that the administrative decision limiting the 9ICD and 10ICD coding of SIDS to ages under one-year was made by WHO in 1979 to influence researchers to focus on younger SIDS because of the increased risk of false positive SIDS in the cohort of one-year and older infants thought to be dying of SIDS. The four ICD8 codes 795, 795.1, 795.2 and 795.3 were used between 1968 and 1978 for: all SIDS at all ages 1968-1972 (before SIDS was first defined); all SIDS < 1 year 1973-1978; all SIDS = 1 year 1973-1978; and all SIDS > 1 year 1973-1978, respectively (See footnote ** to Table 3).

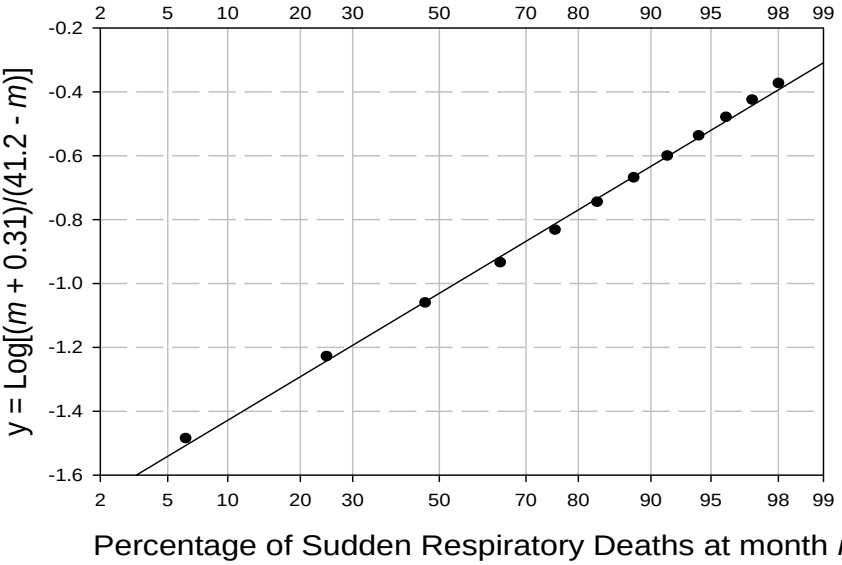
Table 3. Number (*n*) of SIDS and sudden respiratory deaths (SRD) at monthly age attained (*m), for probability distributional analyses at plotting position y**

Data [16]	1 m	2 m	3 m	4 m	5 m	6 m	7 m	8 m	9 m	10 m	11 m	12 m	13-41 m**	Total N
y	-1.487	-1.230	-1.062	-0.936	-0.834	-0.747	-0.670	-0.602	-0.539	-0.481	-0.427	-0.375	-	-
n	3,550	10,496	12,354	10,036	6,436	4,046	2,811	2,007	1,430	940	683	511	1,110	56,410
CDF	0.0629	0.2490	0.4680	0.6459	0.7600	0.8317	0.8816	0.9171	0.9425	0.9592	0.9713	0.9803	1.000	-

**Months may be defined differently by different authors without explanation. see Table 1.*

*** Estimated by semi-logarithm extrapolation of the numbers of deaths at ages 4 to 12 months, out to 41.2 months.*

Figure 1: 4-Parameter Lognormal Distribution (Johnson S_B)
fit to 56,410 ages of Sudden Respiratory Deaths
$y = \text{Log}[(m + 0.31)/(41.2 - m)] = 0.310\, z - 1.031$
where z is a standard normal deviate.



4. CONCLUSION

The probability of SIDS occurring for any given infant at age m can be written, if the risks are independent, as total SIDS risk = $p1\ p2\ p3\ p$G, where risks 1, 2 and 3, as shown above, provide for the age distribution which is the same for males and females and the probability of genetic susceptibility, pG = ~2/3 for males and ~4/9 for females, provides for the binomial gender distribution. By this model, SIDS is inevitable by pure chance and the 4-parameter lognormal distribution of ages results. For every 1000 infants we expect one to be in the highest 10% of severity for each of the three SIDS risk factors of neurological prematurity, respiratory infection and physiological anemia (0.1 x 0.1 x 0.1 = 0.001) which is the order of SIDS risk. Therefore, even though some risk factors can be eliminated (prone sleep position and maternal smoking) or minimized (via education of expectant mothers), the phenomenon of SIDS can be prevented in many cases, but perhaps not in all of them. This is because "term infants from non-smoking, rich families who sleep in the supine position also die of SIDS, just not as frequently [28]." The X-linkage model may have an input for genetic counseling if proven, given that a mother of a male or female SIDS has a slightly higher risk (3/4 as opposed to 2/3) of passing a recessive allele to her subsequent child because she cannot be dominant-dominant.

We have previously shown that SIDS has a mathematically rigid structure of its age and gender distributions that apply to all developed countries where high medical standards of autopsy are maintained [18]. This analysis implies that genetic work should be done on SIDS cases to find an X-linked gene with two alleles ($p \approx 1/3$ and $q \approx 2/3$) with the protective dominant allele virtually missing in SIDS and the recessive allele appearing in virtually all SIDS (assuming no false positive infanticide cases reported as SIDS).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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