

# Sudden Infant Death Syndrome: Research and Risk Reduction



**Thomas G. Keens, M.D.**

**Chair, California SIDS Advisory Council**

**Professor Emeritus of Pediatrics, Physiology and Neuroscience  
Keck School of Medicine of the University of Southern California**

**Division of Pediatric Pulmonology and Sleep Medicine  
Children's Hospital Los Angeles**



**No Conflicts of Interest to Disclose**





**“And this woman's son  
died in the night ...”**

**1 Kings 3: 19  
(950 B.C.)**



LAPSE OF TIME FROM MOMENT WHEN LAST SEEN ALIVE TO THE DISCOVERY OF DEATH (96 Cases)

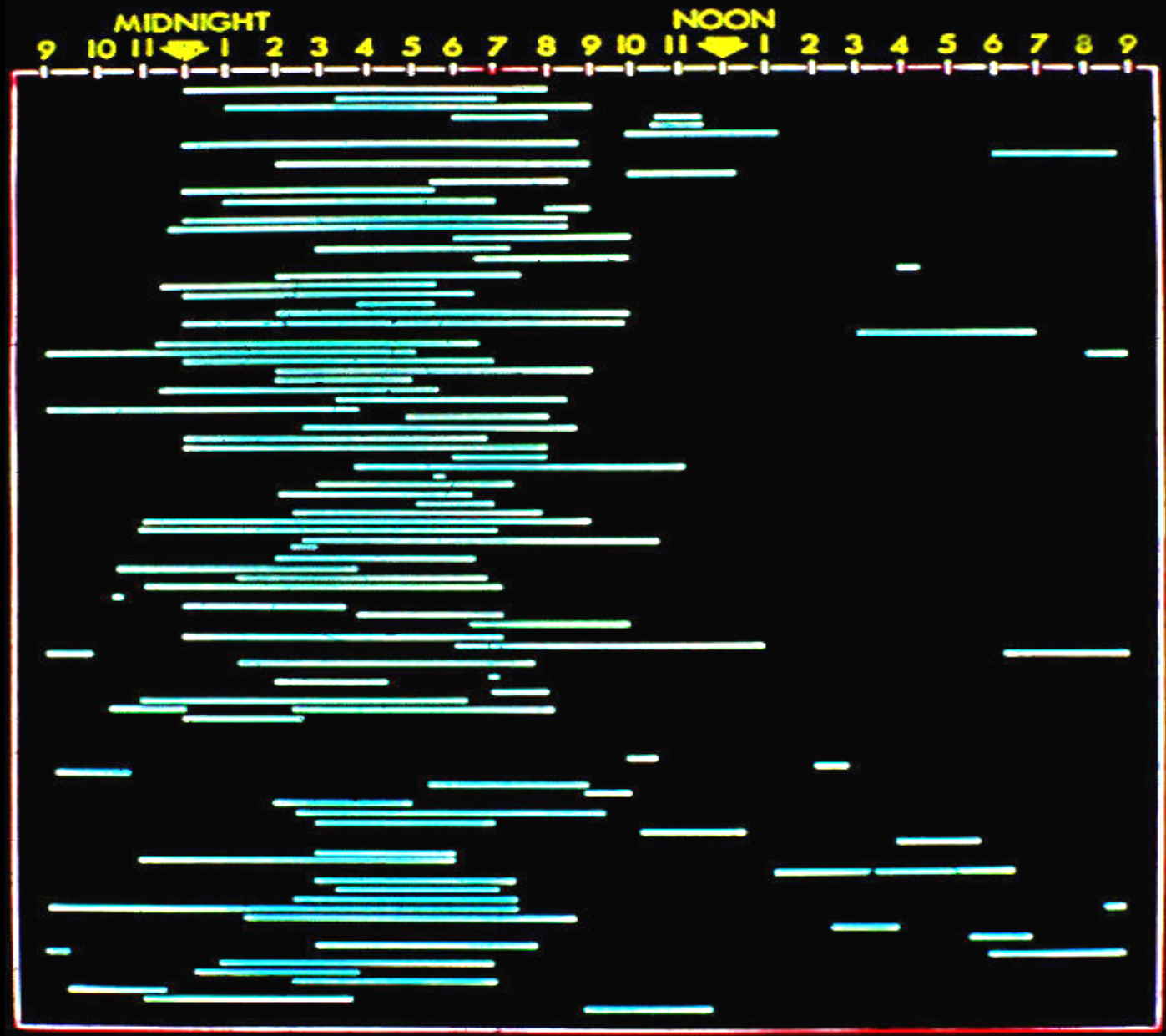


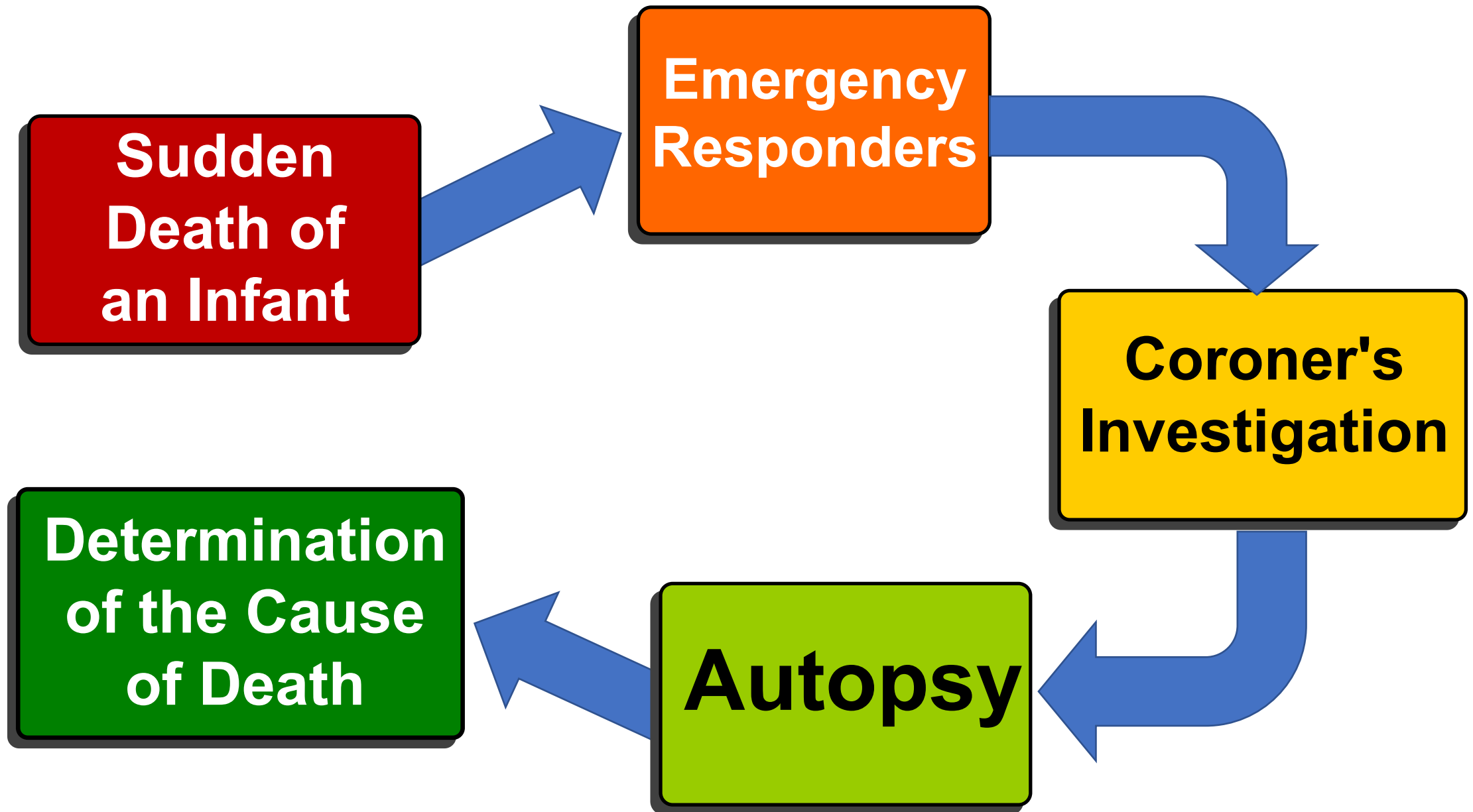
Figure Courtesy of Doctor Maria Valdes-Dapena



**ACTION 10**  
HD NEWS

# Baby Death Investigation

1400 blk of Corban



**The sudden unexpected death of an infant, under one-year of age, with onset of the fatal episode apparently occurring during sleep, that remains unexplained after a thorough investigation, including performance of a complete autopsy, and review of the circumstances of death and the clinical history.**



**Krous, H.F., J.B. Beckwith, R.W. Byard, T.O. Rognum, T. Bajanowski, T. Corey, E. Cutz, R. Hanzlick, T.G. Keens, and E.A. Mitchell. *Pediatrics*, 114: 234-238, 2004.**

- From blaming parents, Ancient Greece and Rome through the Middle Ages.
- To natural causes, Late 1800's and early 1900's.
- To blaming parents again, Early to mid 1900's.
- To natural causes again, Late 1900's and early 2000's.
- Now to unsafe, accidental causes.



# Different Coroners Use Different Diagnoses for these Infants



**When diagnosing the cause of death in an infant dying suddenly and unexpectedly during sleep, the following terms are considered synonymous:**

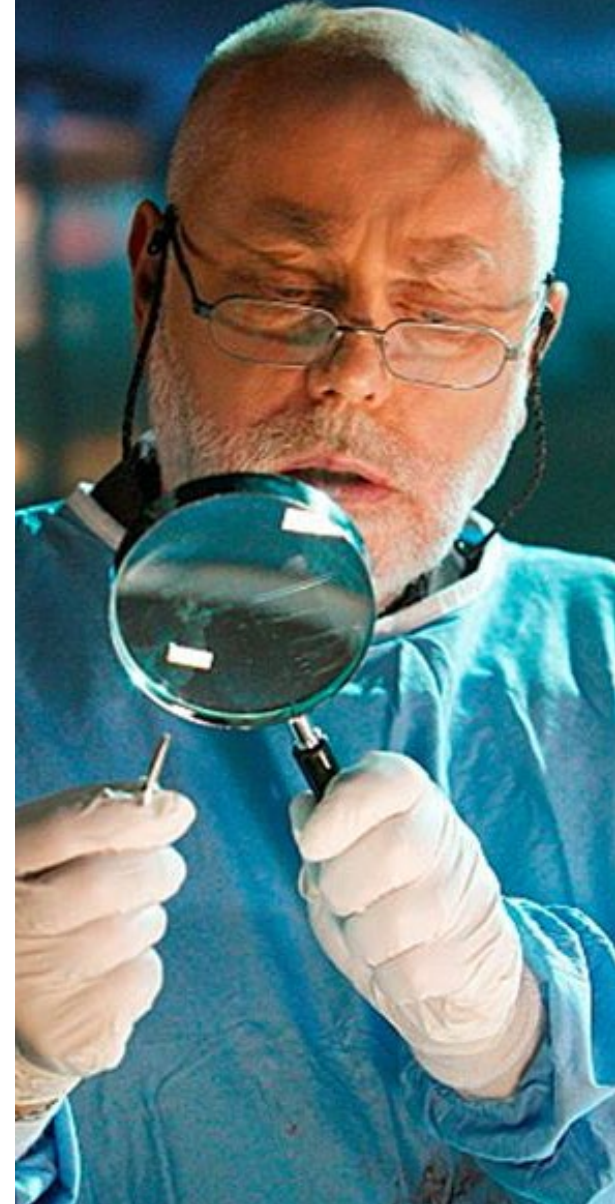
- **SIDS**
- **SUID**
- **SUDI**
- **Undetermined**

**They all mean the same thing; that the infant's death is *unexpected* and *unexplained*.**

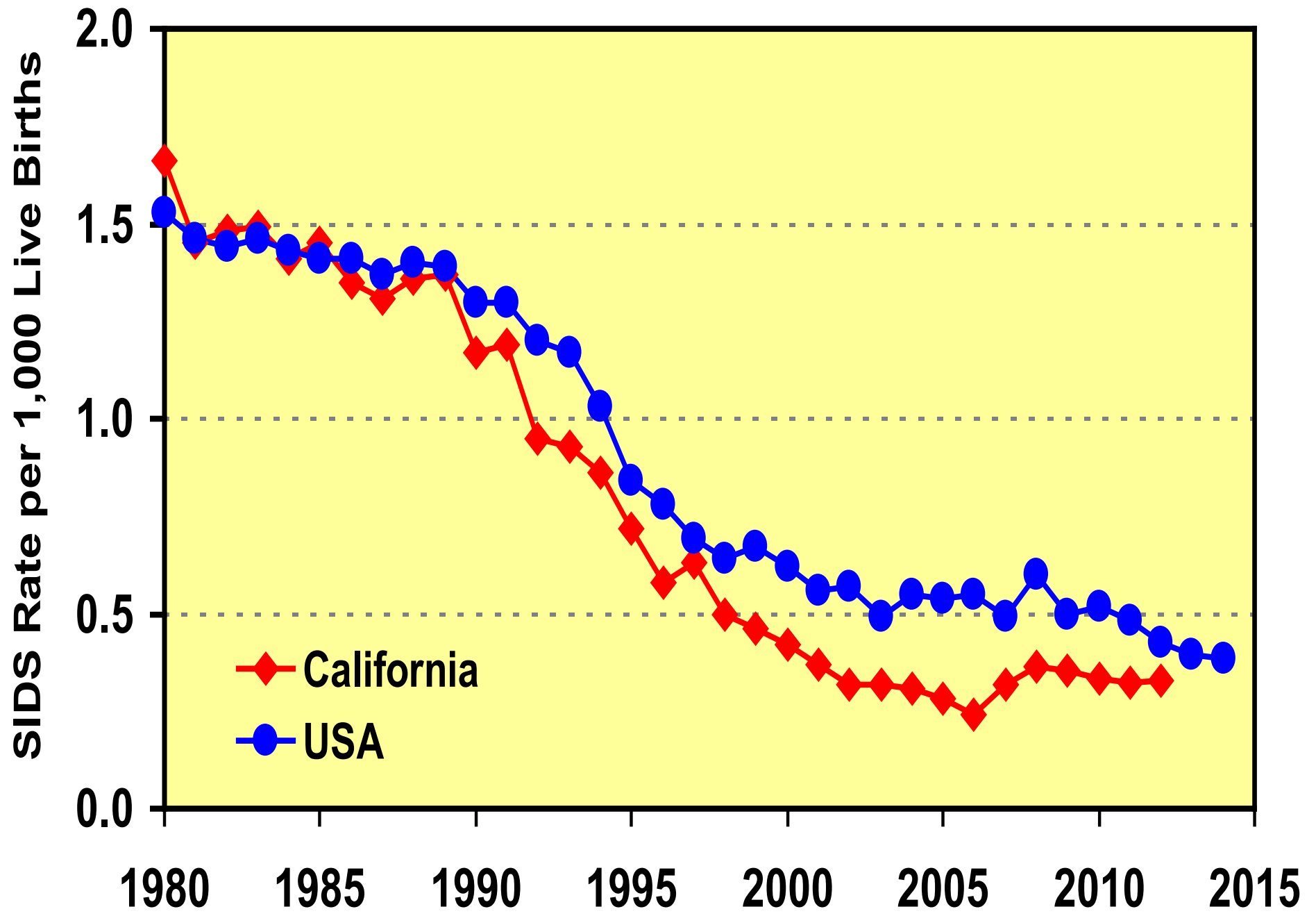
Krous, H.F. *Forensic. Sci. Med. Pathol.*, 9: 91–93, 2013.

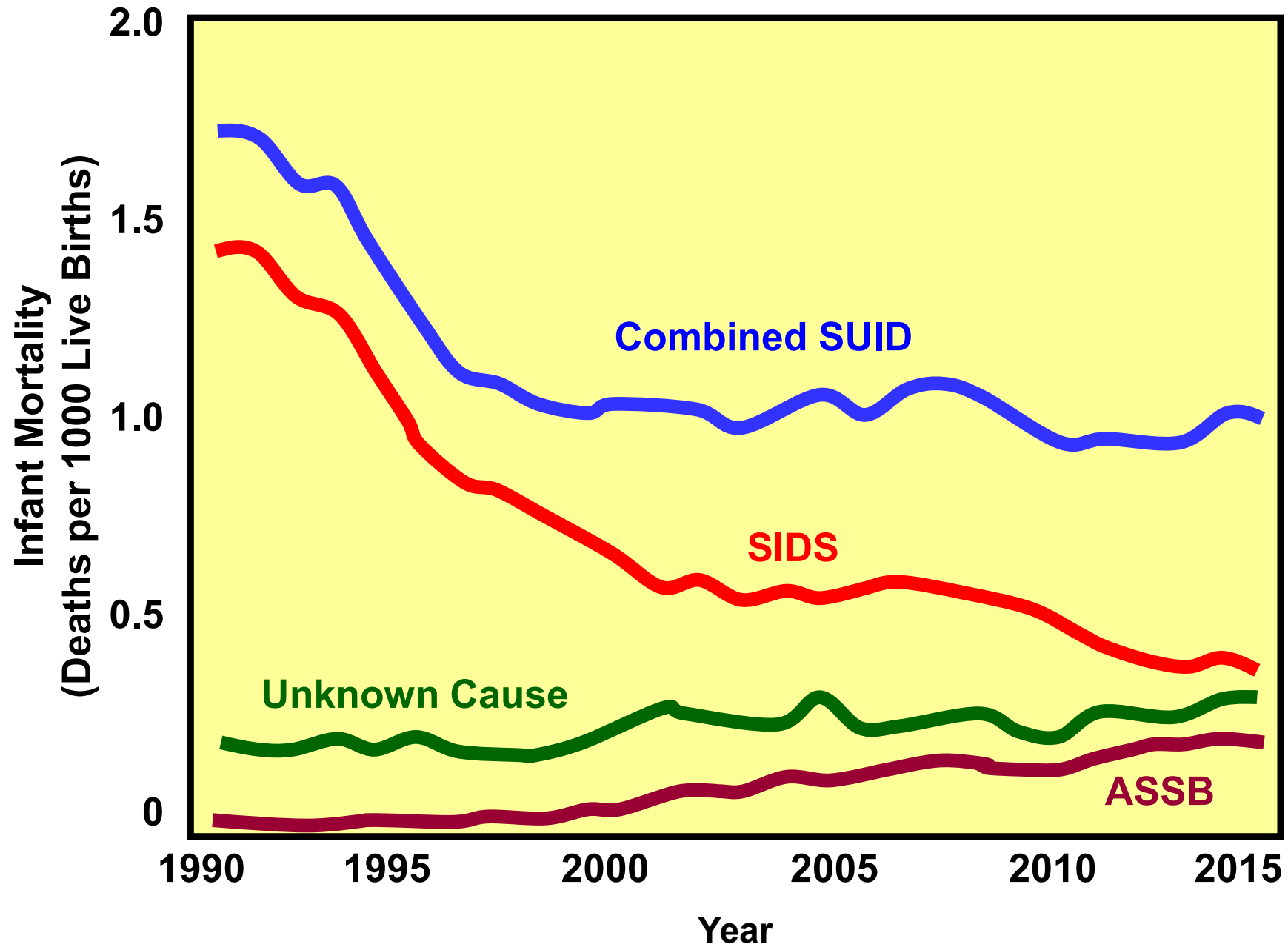
Cutz, E. *JAMA Pediatr.*, 170: 315-316, 2016.

Goldstein, R.D., et al. *For. Sci. Med. Pathol.*, doi: 10.1007/s12024-019-00156-9, 2019.



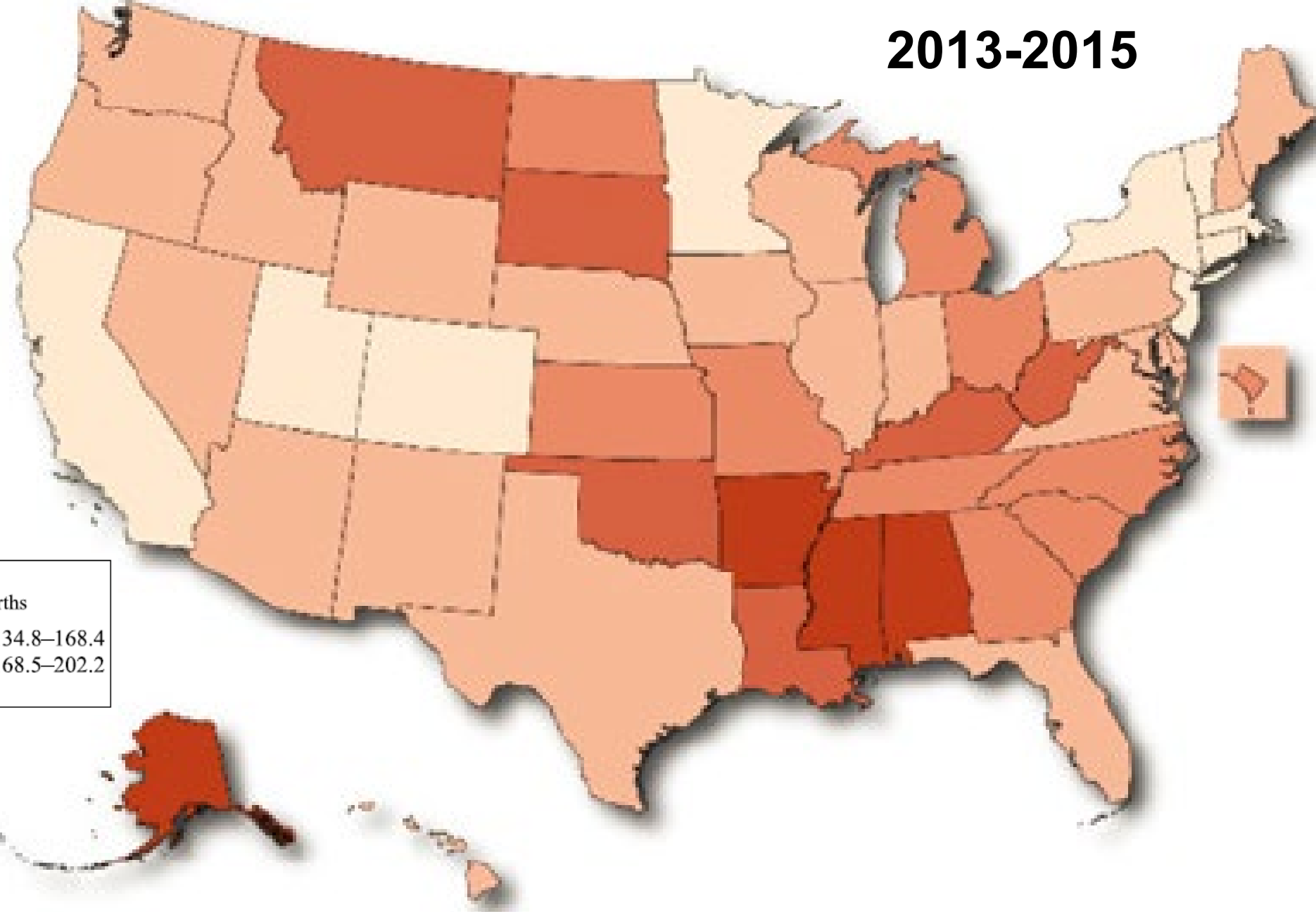




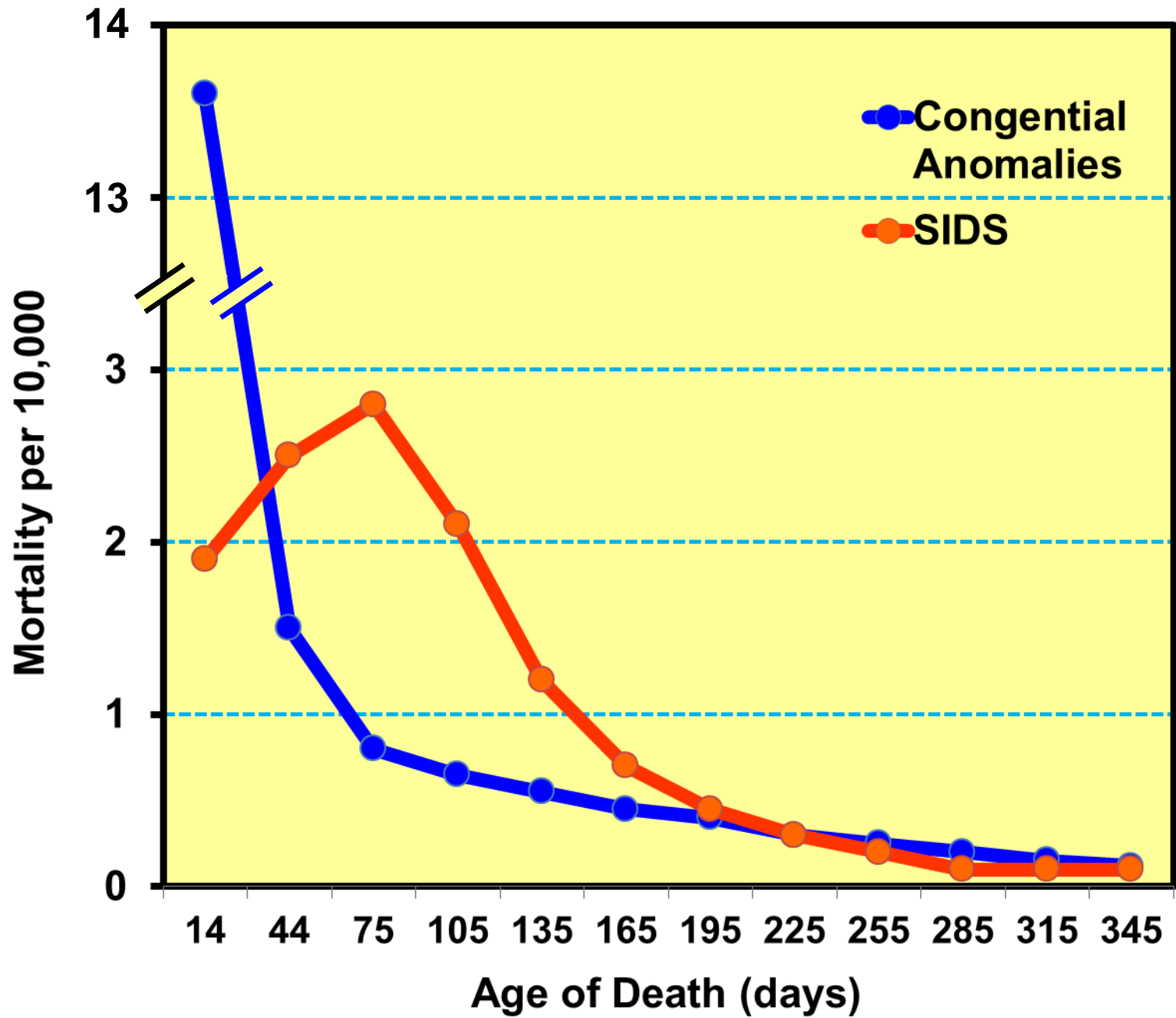


Erck Lambert, A.B., et al. *Pediatrics*, 141: doi:10.1542/peds.2017-3519 , 2018.

2013-2015

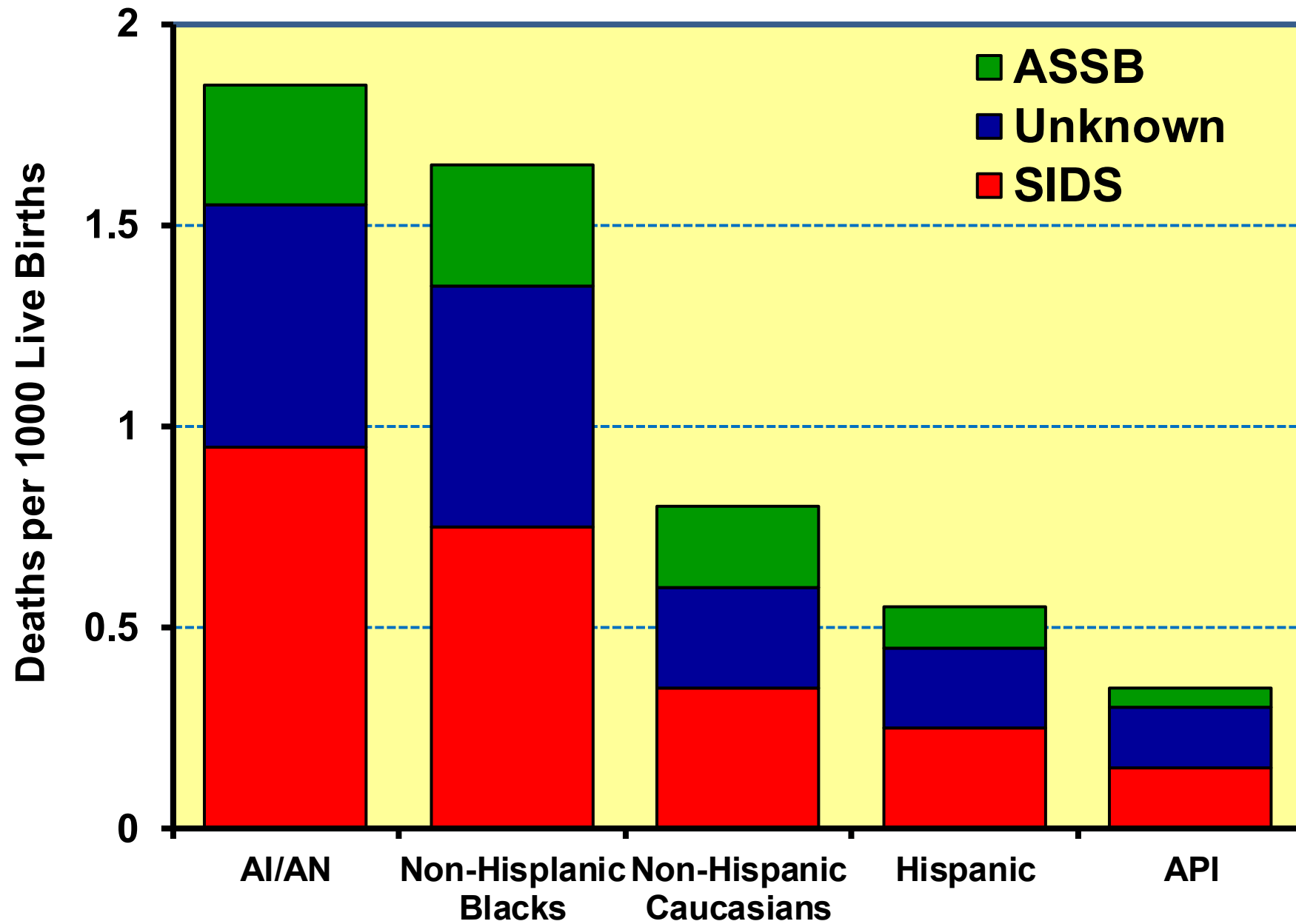


SUID rate per 100000 live births	
33.3–67.1	134.8–168.4
67.2–100.9	168.5–202.2
101.0–134.7	

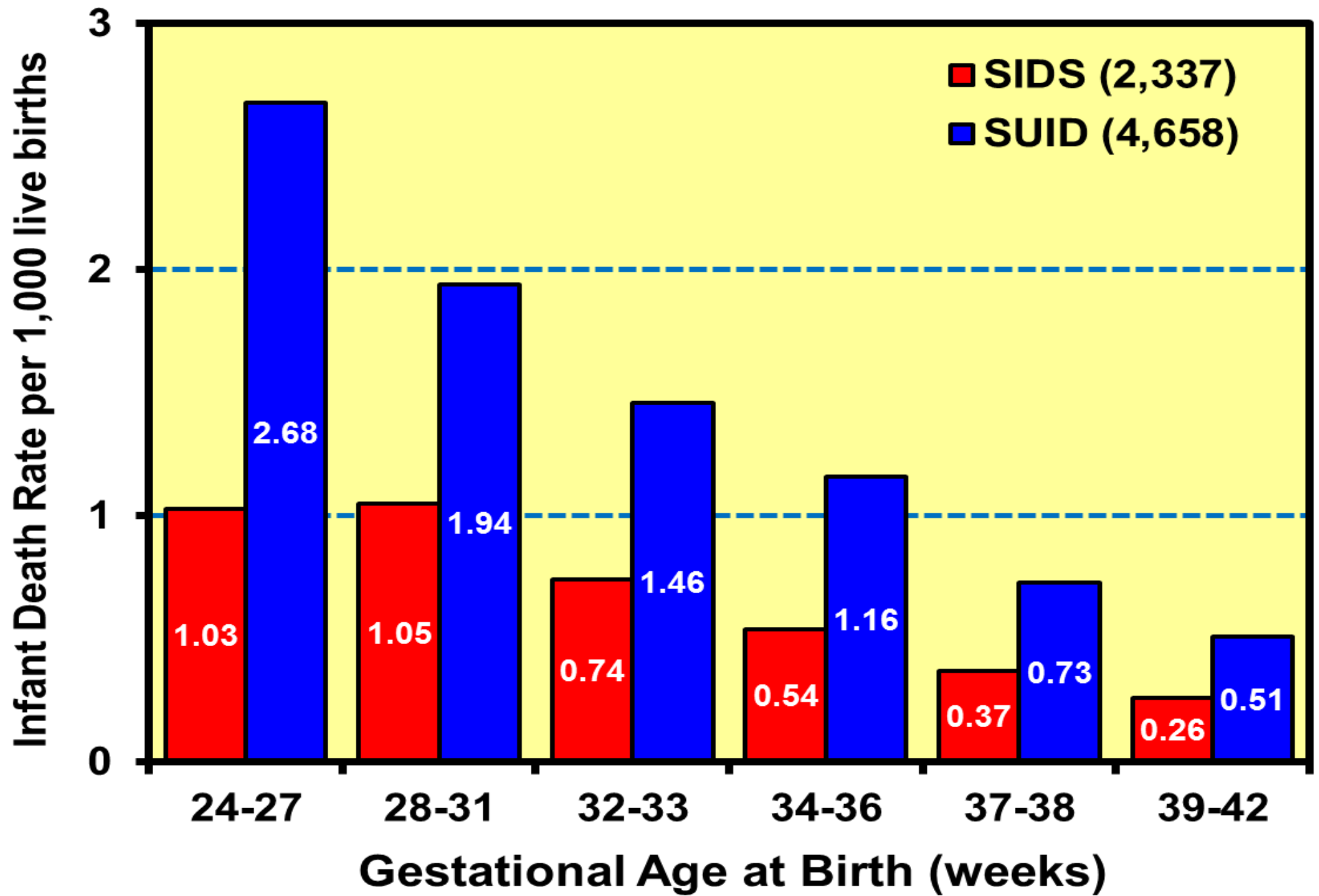


Guntheroth, W.G., and P.S. Spier. *Pediatrics*, 110: 110;e64, 2002.

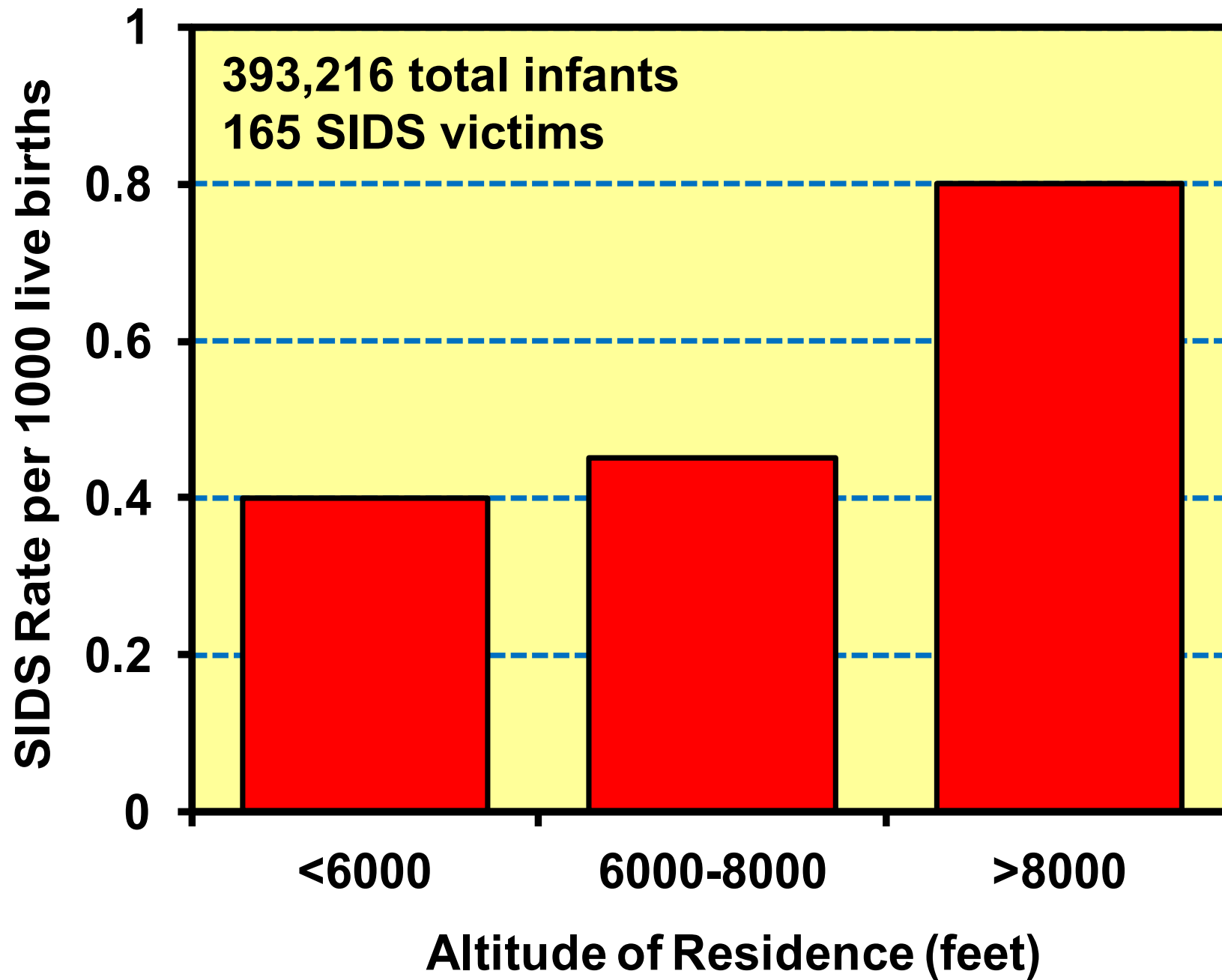




<https://www.cdc.gov/sids/data.htm>



Ostfeld, B.M., et al. *Pediatrics*, 140: e20163334, 2017.



- **No identifiable cause of death.**
- **No signs of severe illness.**
- **No signs of significant stress.**
- **Diagnosis of exclusion**



**Imagine a car driving up a  
steep mountain road.**

**The car has stopped.**

**Why can't the car continue  
up the hill?**

Imagine a car driving up a steep mountain road. The car has stopped. Why can't the car continue up the hill?

## Medical Model.

- There is a flat tire.
- Identify the problem.
- Find a solution to the problem.
- Fix the problem.

- **Cardiac causes.**
- **Respiratory causes.**
- **Arousal disorders.**
- **Metabolic disorders.**
- **Infections.**
- **Vitamin deficiency.**
- **Environmental toxins.**

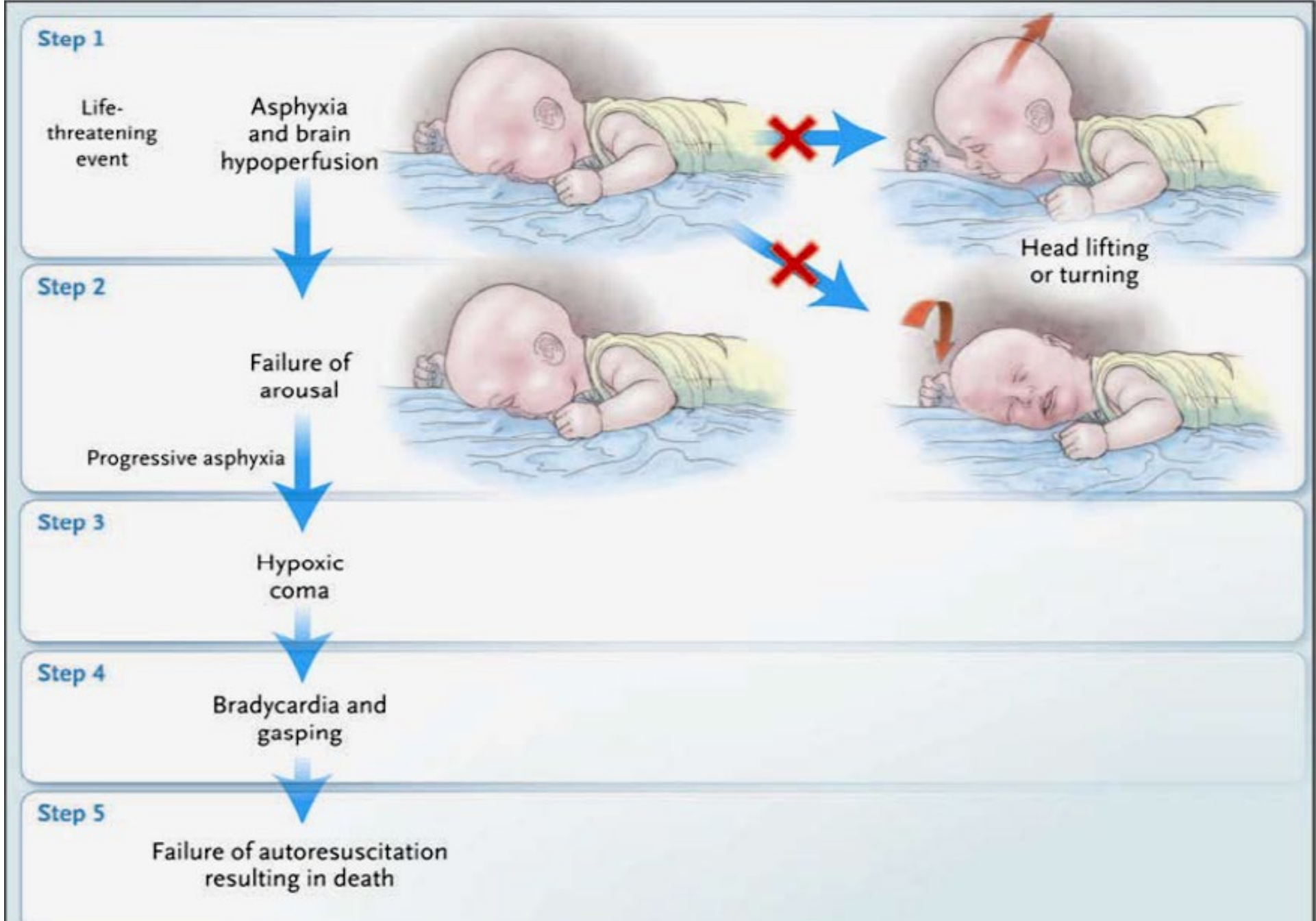


Imagine a car driving up a steep mountain road. The car has stopped. Why can't the car continue up the hill?

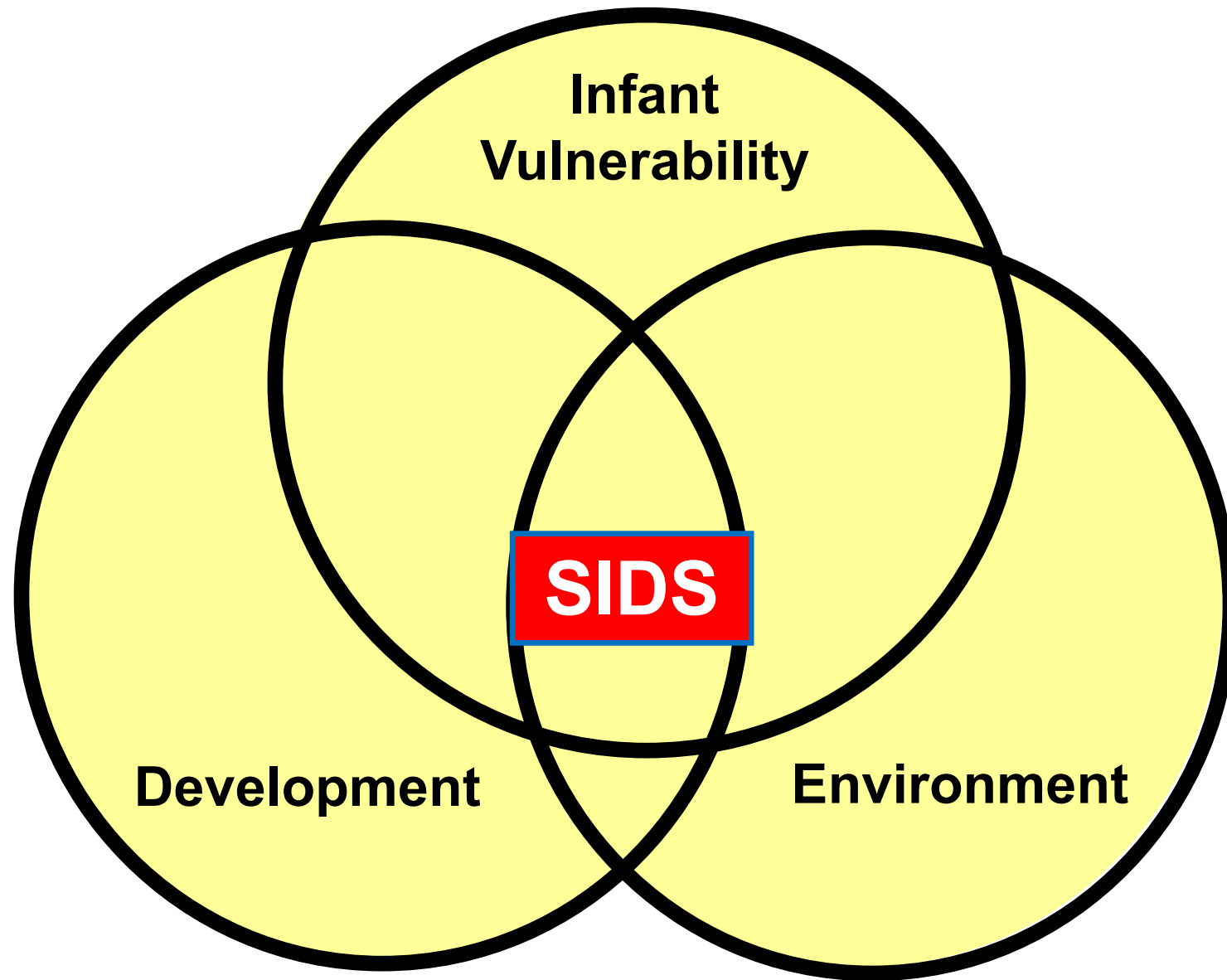
## **A New Way of Thinking.**

- There are too many passengers.
- The engine is not powerful enough.
- The road is too rocky.
- The road is too steep.

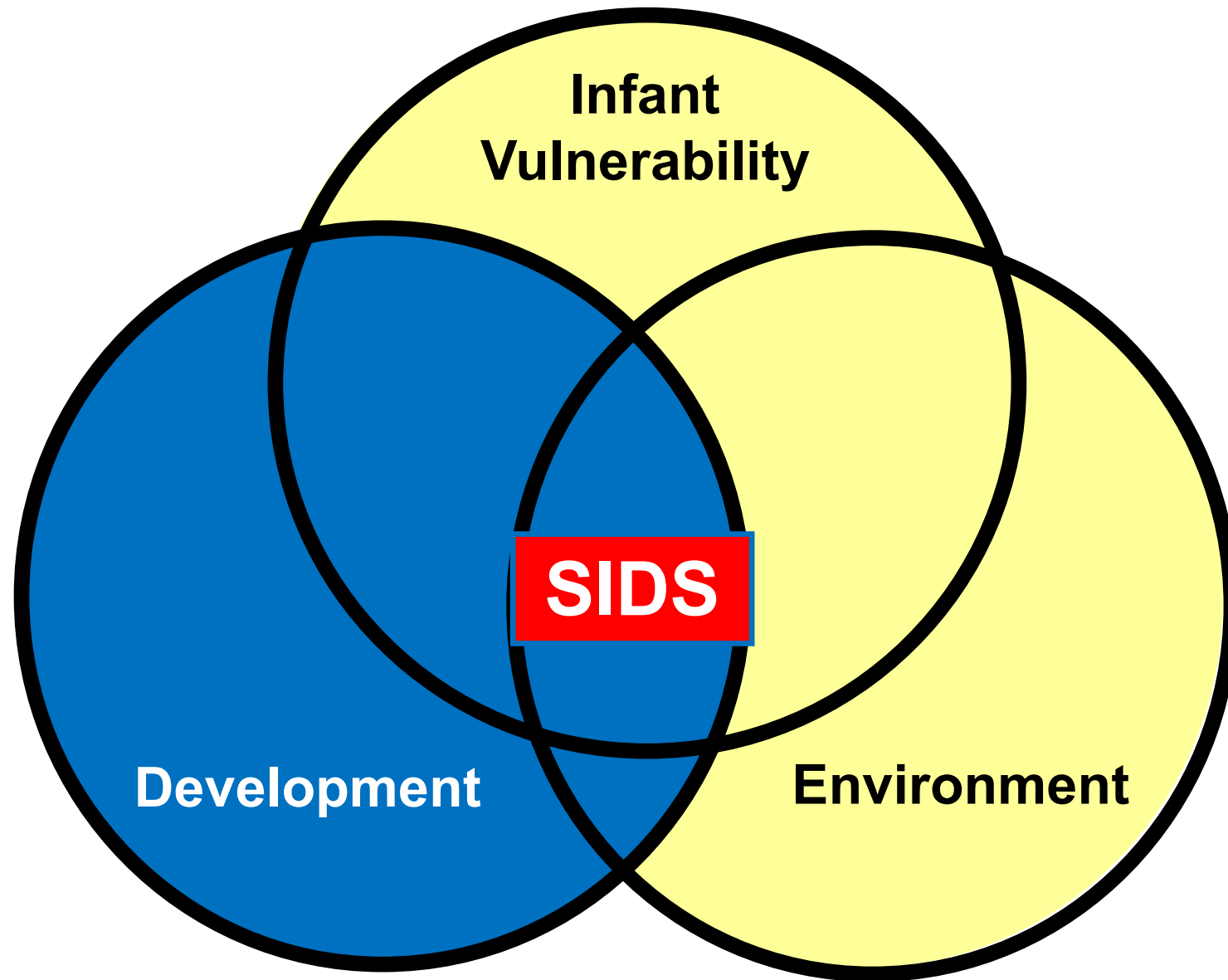




Kinney, H.C., and B.T. Thach. *N. Eng. J. Med.*, 361: 795-805, 2009.



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.

# Developing Infant Cardiorespiratory Physiology is Unstable



- **Any system in transition is intrinsically unstable.**
- **Infant cardiorespiratory physiology undergoes rapid changes in the first 3-6 months of life.**
- **Thus, infant physiological responses are immature and do not function optimally.**

- **Clinical Sites.**
  - **Los Angeles, California.**
  - **Chicago, Illinois.**
  - **Honolulu, Hawaii.**
  - **Cleveland, Ohio.**
  - **Toledo, Ohio.**
- **Clinical Trial Operation Center.**
- **Data Coordinating and Analysis Center.**
- **NICHD.**

- **Clinical Sites.**
  - **Los Angeles, California.**
  - **Chicago, Illinois.**
  - **Honolulu, Hawaii.**
  - **Cleveland, Ohio.**
  - **Toledo, Ohio.**
- **Clinical Trial Operation Center.**
- **Data Coordinating and Analysis Center.**
- **NICHD.**





# CHIME Steering Committee

NICHD, Bethesda, Maryland, U.S.A. *July, 1992.*





# CHIME Steering Committee

NICHD, Bethesda, Maryland, U.S.A. *July, 1992.*

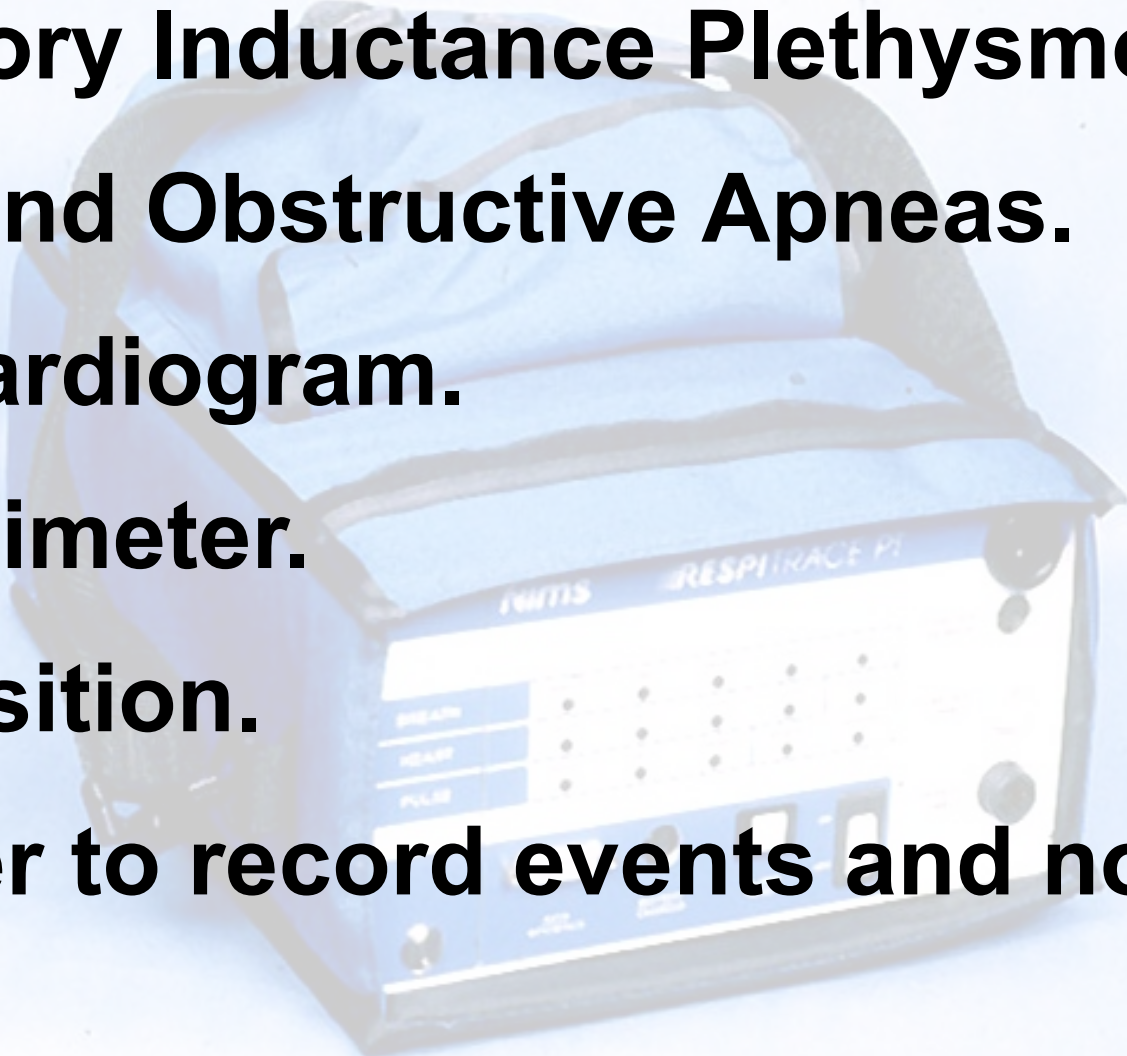


**USC**  
University of  
Southern California

# The CHIME Study

<b>Healthy Term Infants</b>	<b>Home monitoring up to 66 wks PCA (age 6 months).</b>
<b>Preterm Infants</b>	<b>Home monitoring up to 56 wks PCA (age 4 months).</b>
<b>ALTE Infants</b>	<b>Until infant has no real alarms for 3-months.</b>
<b>SIDS Siblings</b>	<b>Until 66 wks PCA, or 4 wks past age of death of SIDS.</b>



- **Respiratory Inductance Plethysmography.**
  - **Central and Obstructive Apneas.**
  - **Electrocardiogram.**
  - **Pulse Oximeter.**
  - **Body Position.**
  - **Computer to record events and normative data.**
- 

Neuman, M.R., et al., and CHIME. *Physiol. Meas.*, 22: 267-286, 2001.  
Ramanathan, R., and CHIME. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.



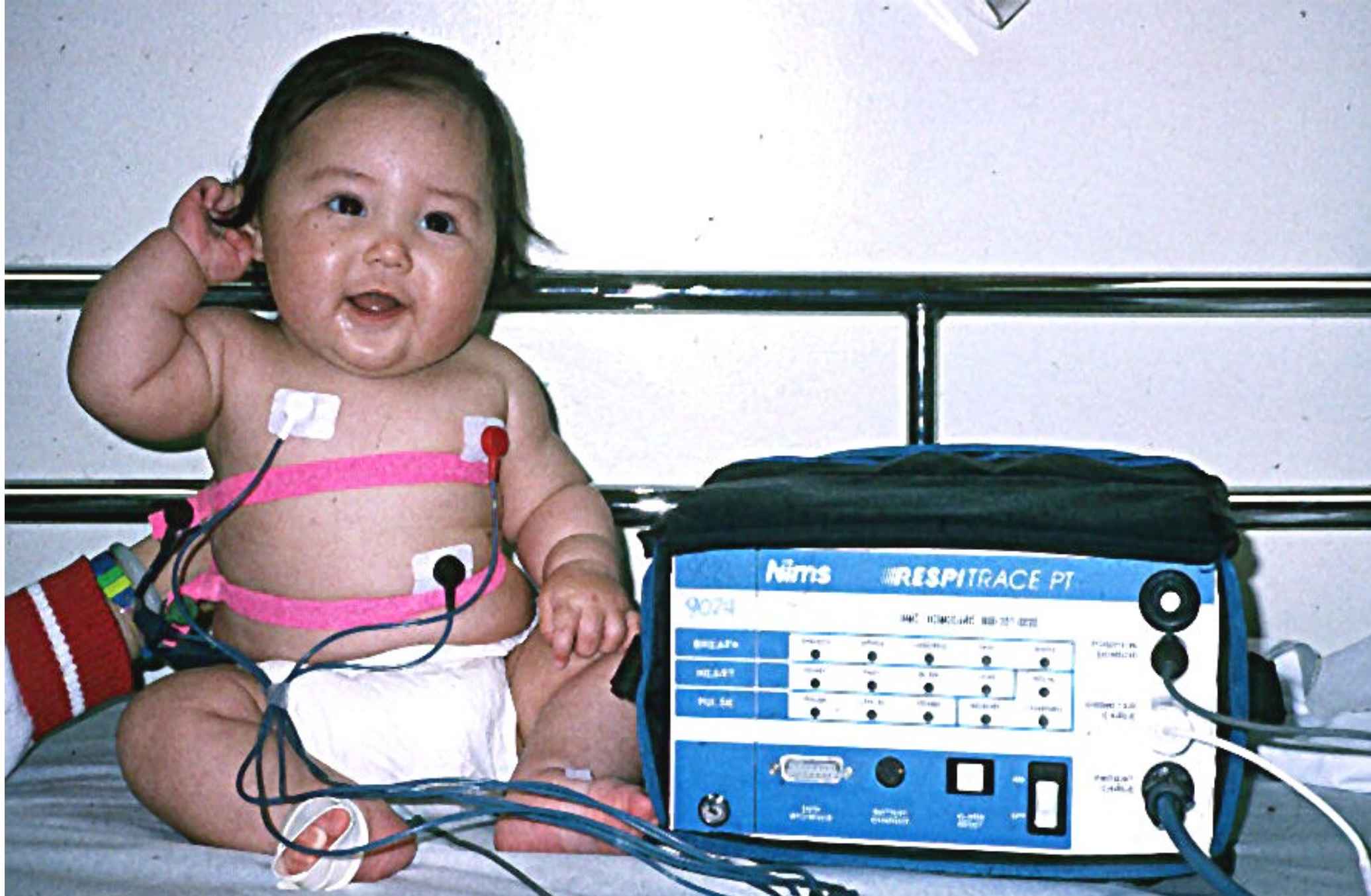
The CHIME Home Monitor (Non Invasive Monitoring Systems, Miami, Florida, U.S.A.)

Neuman, M.R., et al., and CHIME. *Physiol. Meas.* 22: 267-286. 2001.



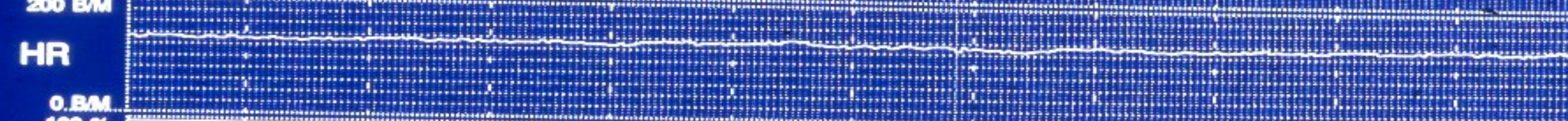
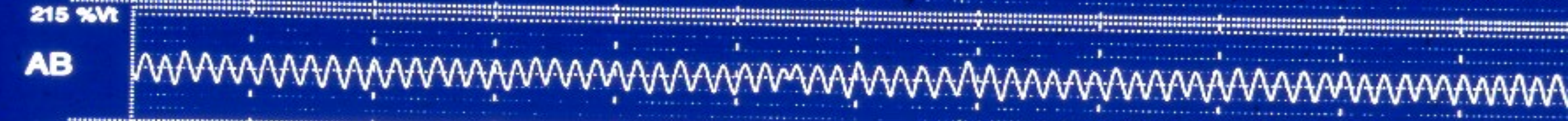
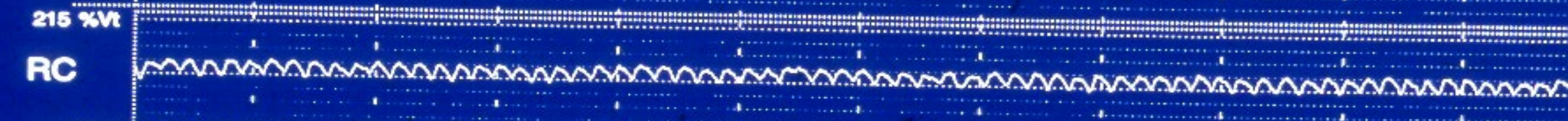
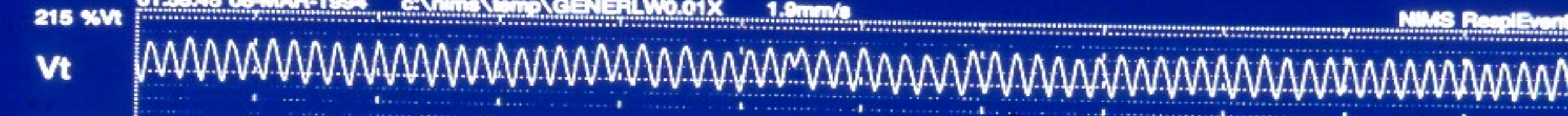
Neuman, M.R., et al., and CHIME. *Physiol. Meas.*, 22: 267-286, 2001.



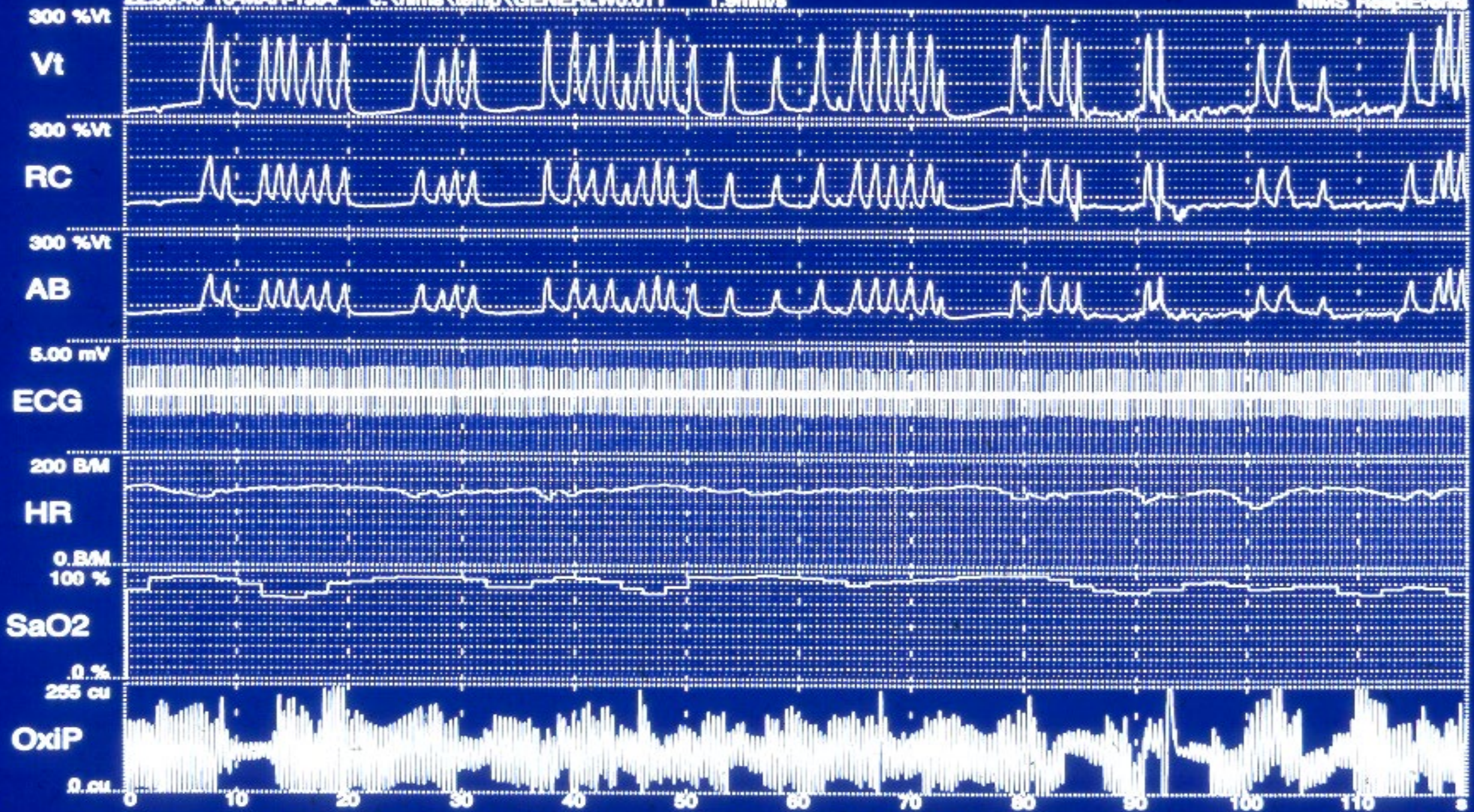


Neuman, M.R., et al., and CHIME. *Physiol. Meas.*, 22: 267-286, 2001.

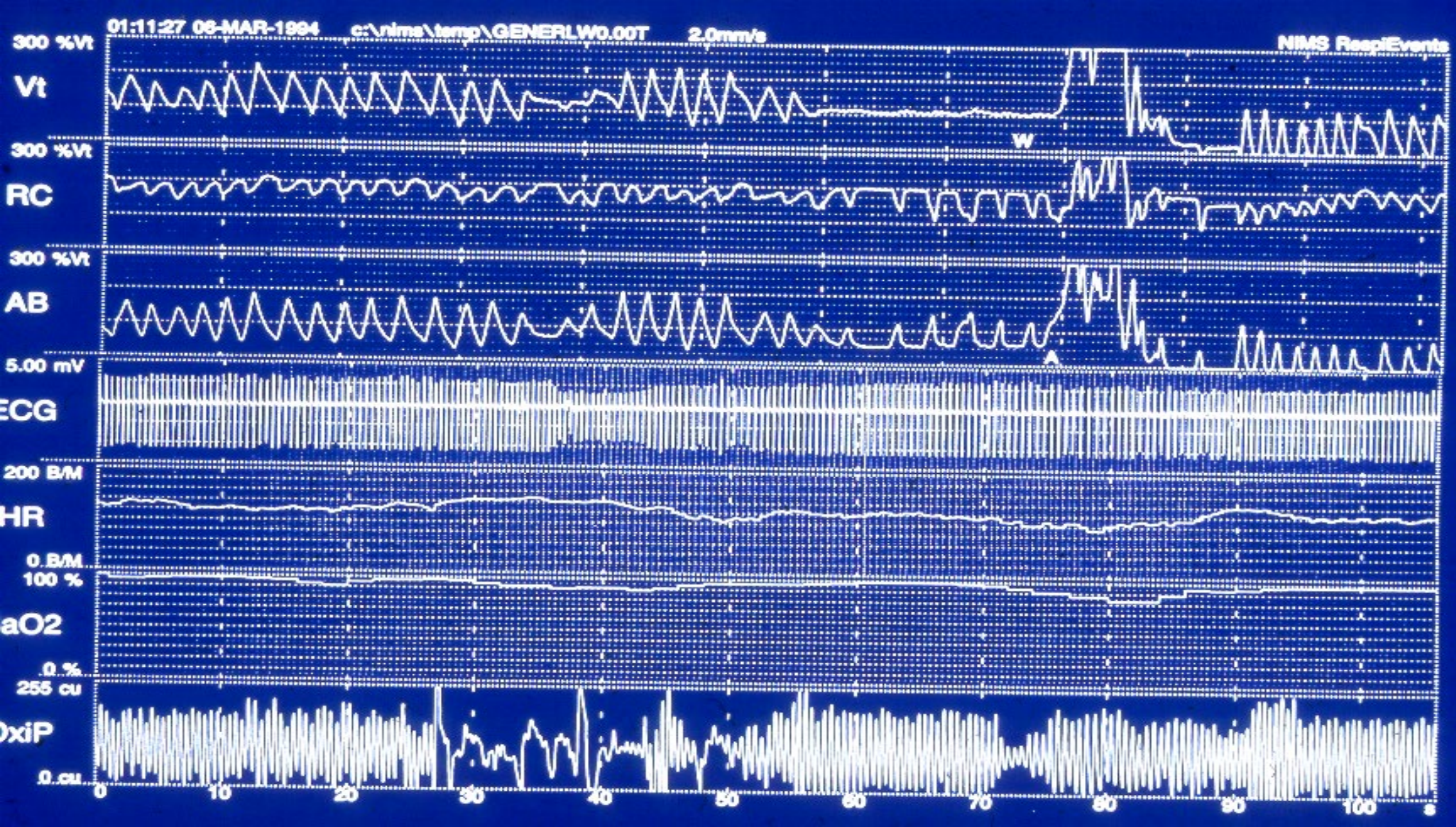








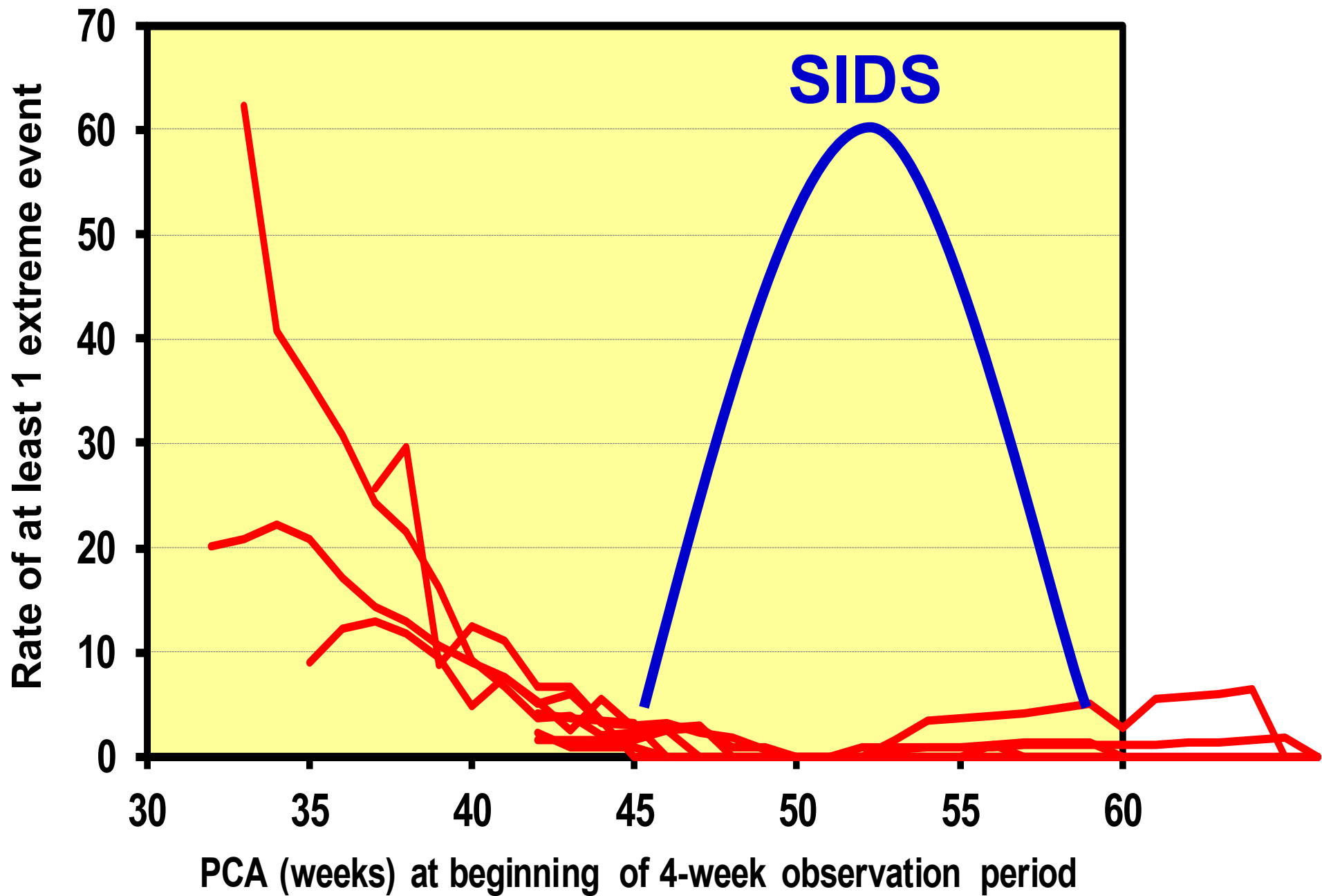






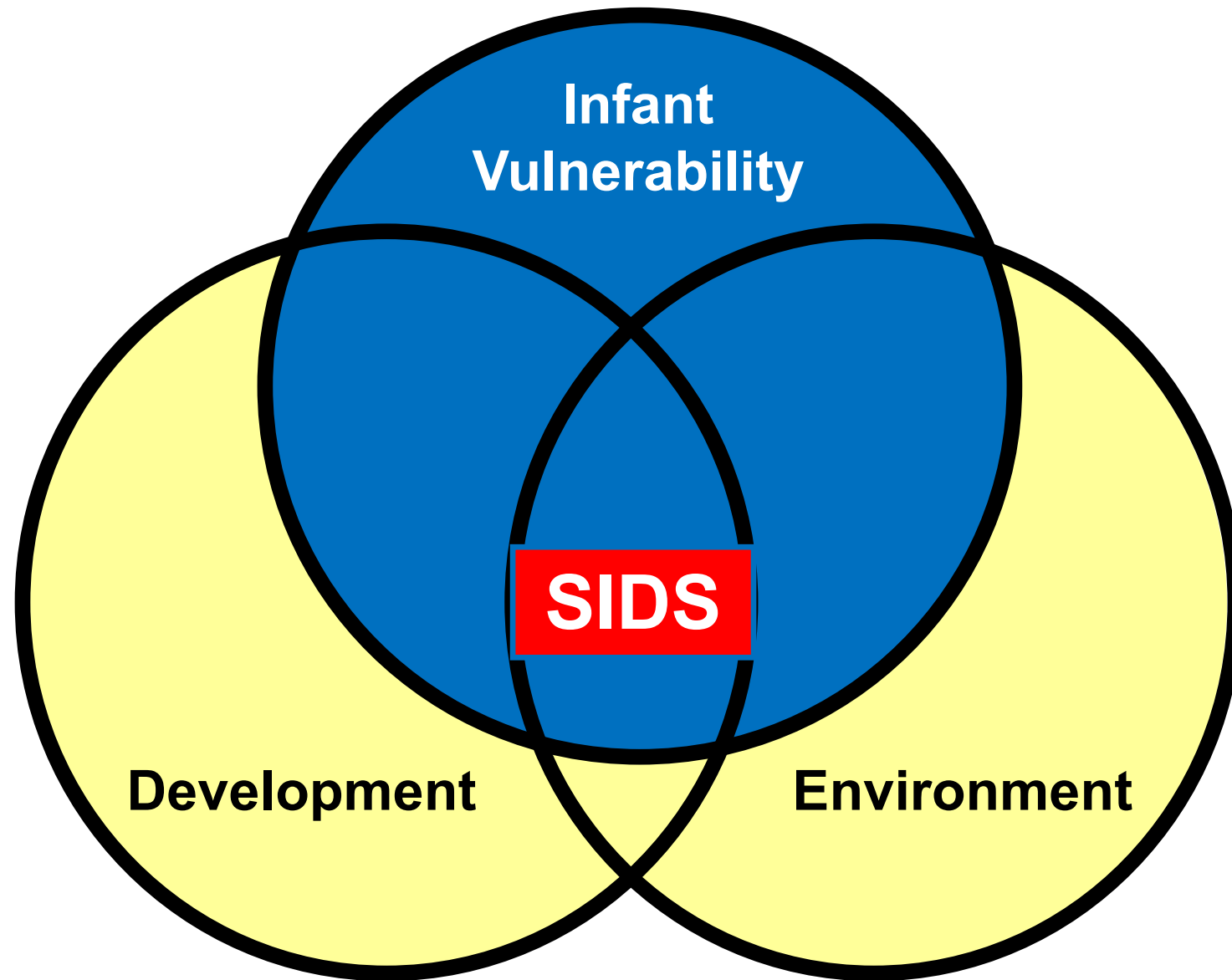
# Is SIDS a Catastrophic Physiologic Crisis?

- **If normal infants do not precisely control breathing, heart rate, and oxygenation ...**
- **Then SIDS may not have to be a catastrophic physiological crisis.**
- **Maybe it just needs to be a small problem which nudges or pushes a vulnerable infant over the edge.**

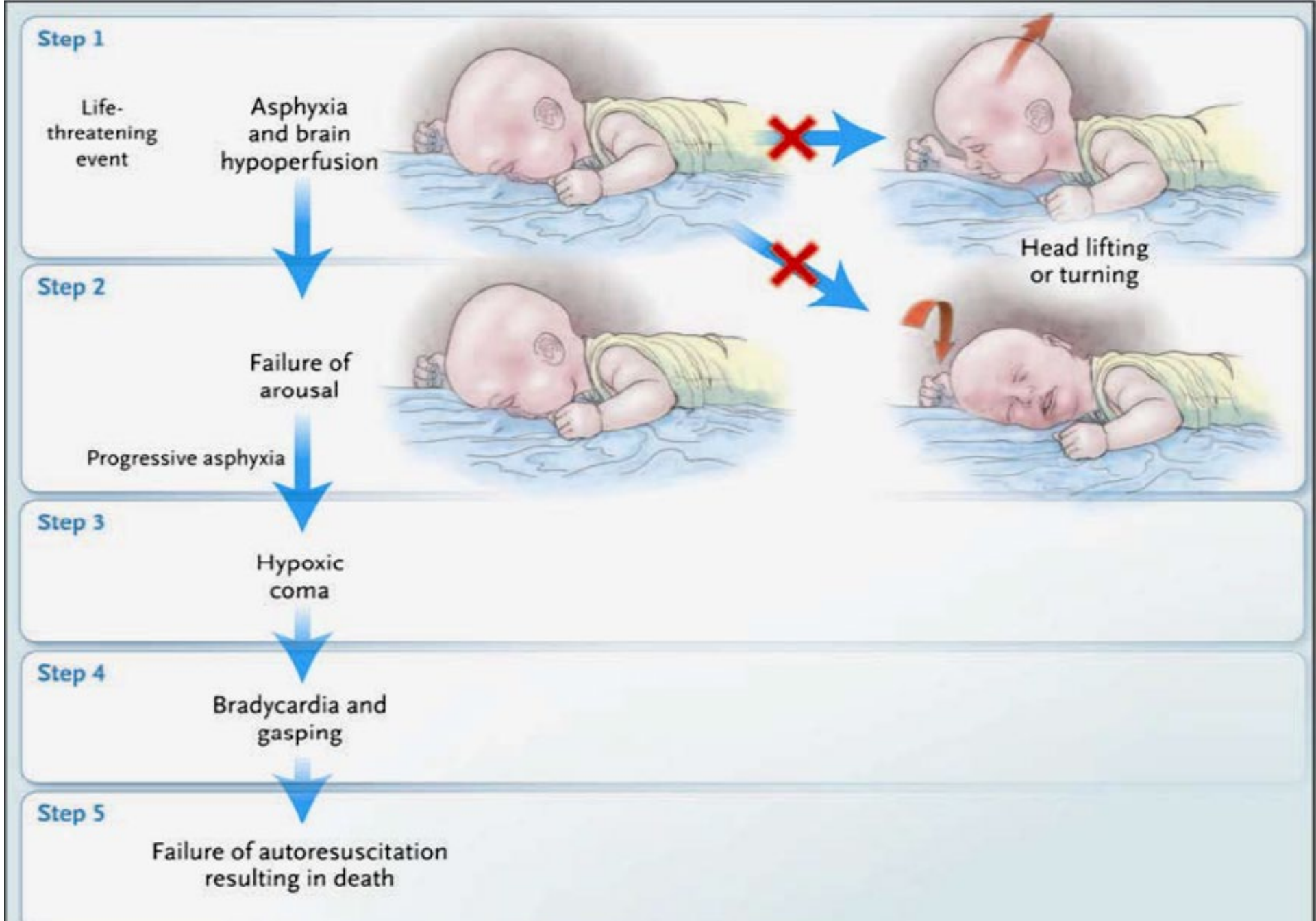


Ramanathan, R., and CHIME. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.

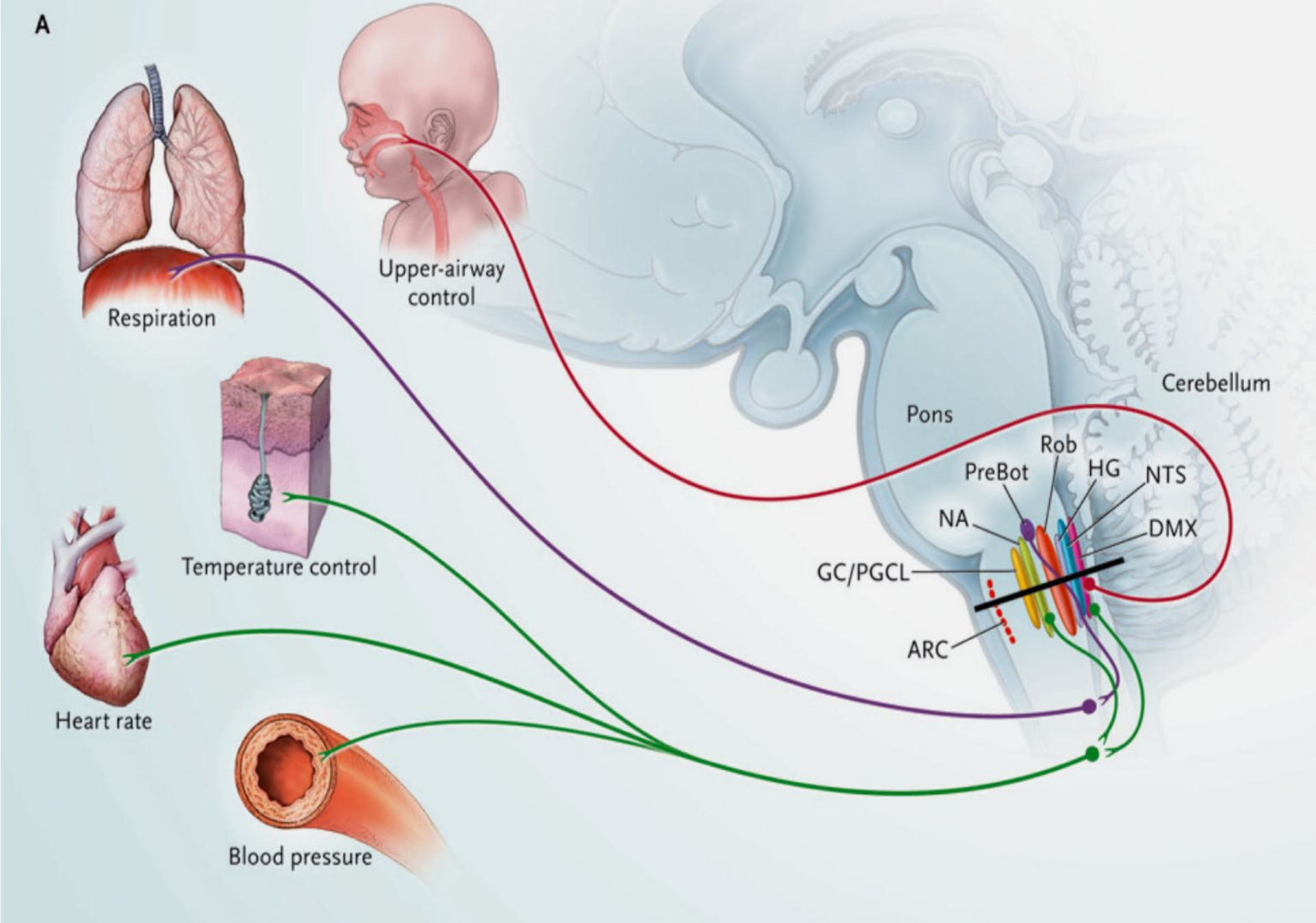




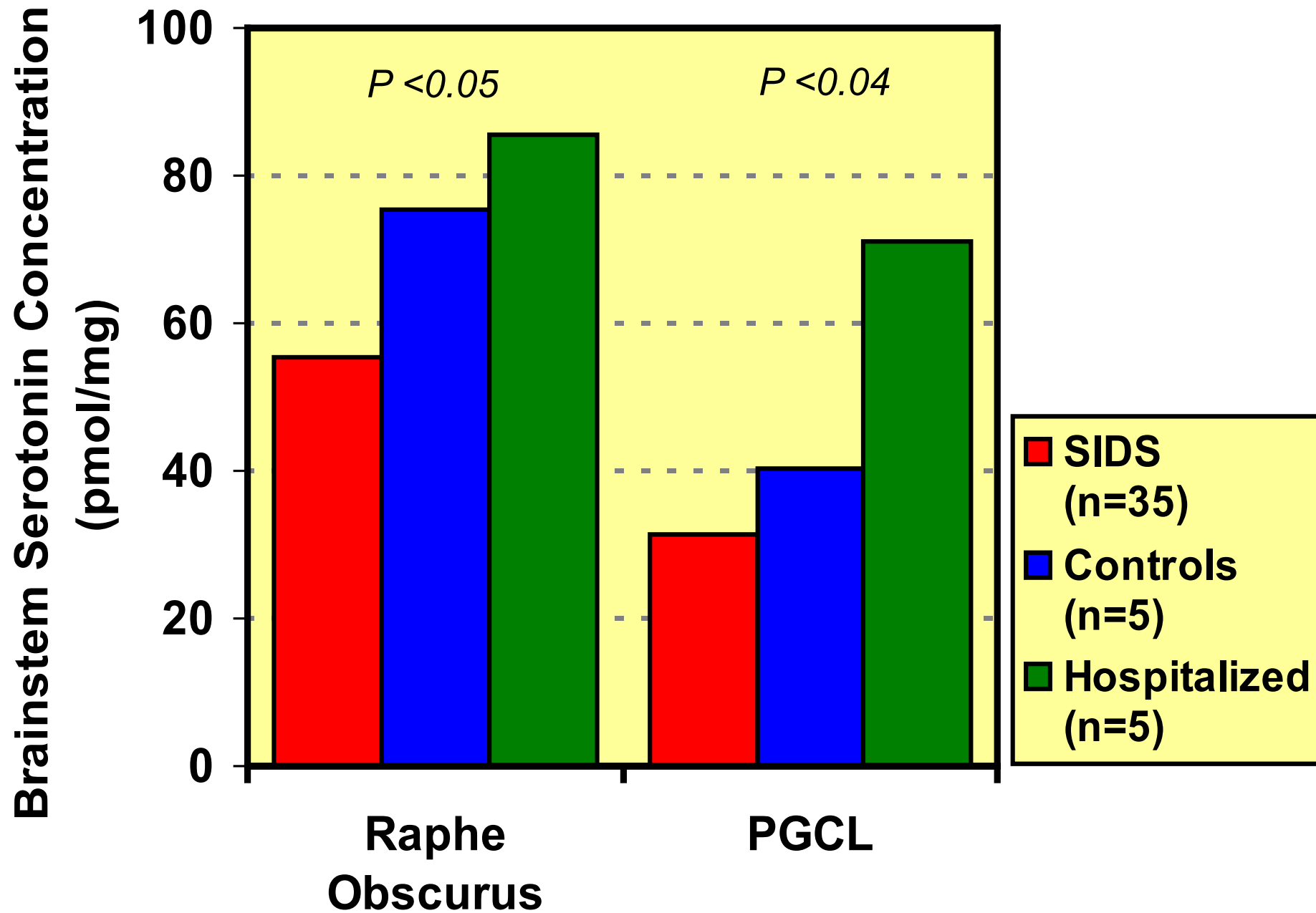
Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.



Kinney, H.C., and B.T. Thach. *N. Eng. J. Med.*, 361: 795-805, 2009.



**Kinney, H.C., and B.T. Thach. *N. Eng. J. Med.*, 361: 795-805, 2009.**

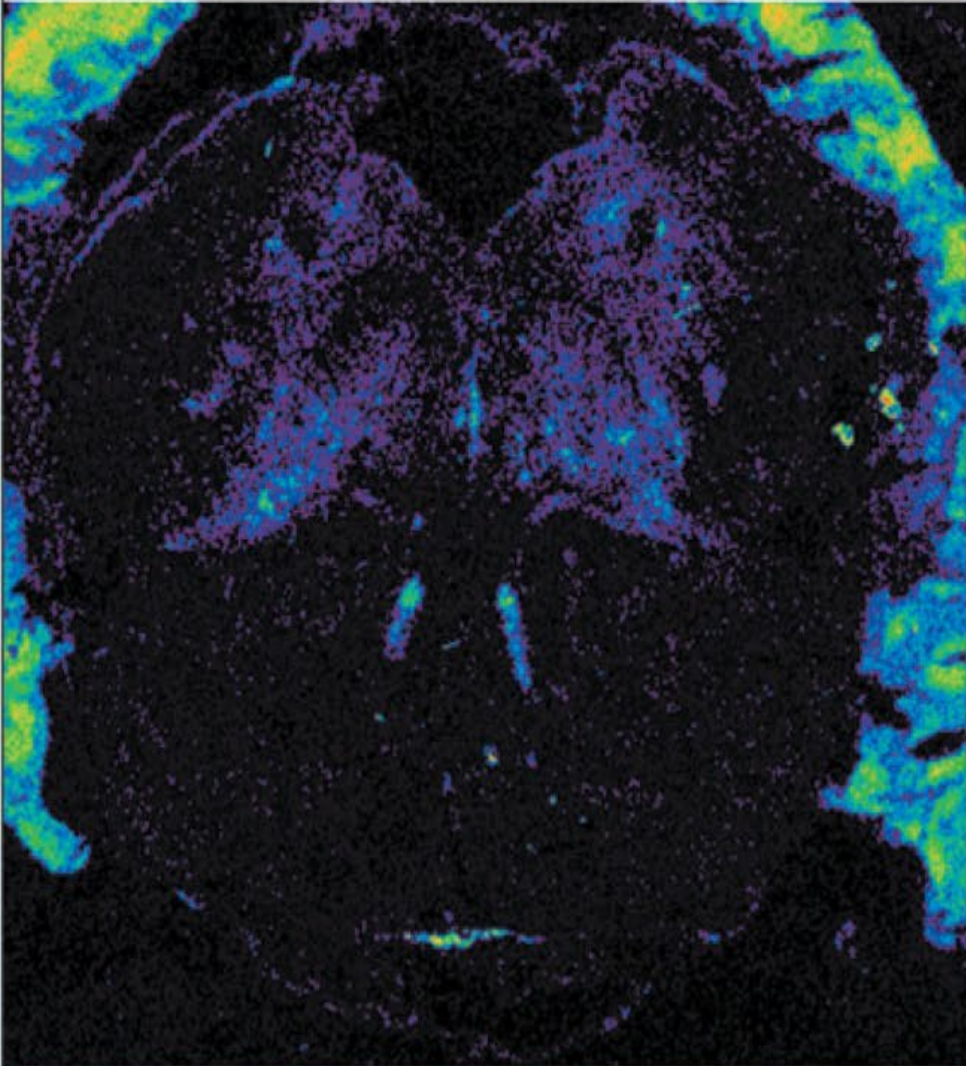




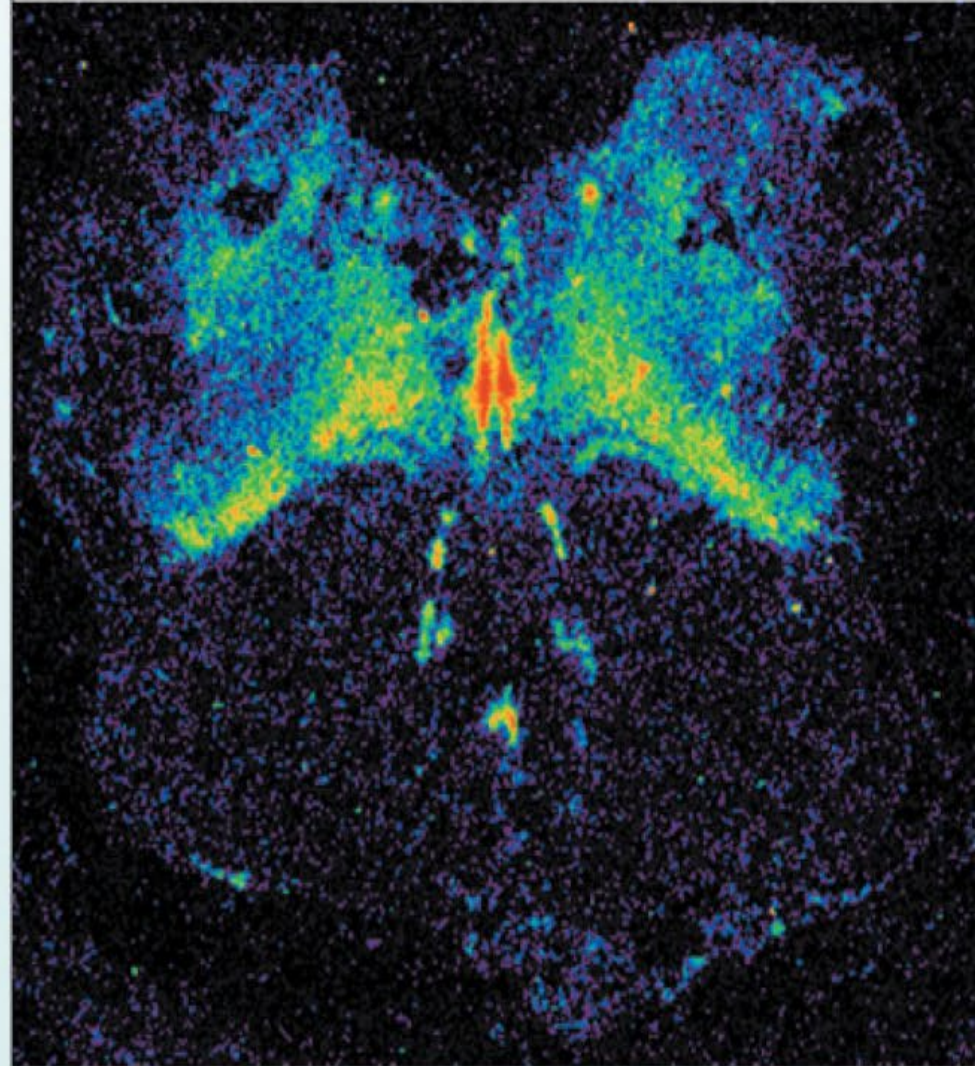
# 5-HT<sub>1A</sub> Receptor Binding Density in SIDS Brainstems



**B** Infant with Sudden Infant Death Syndrome



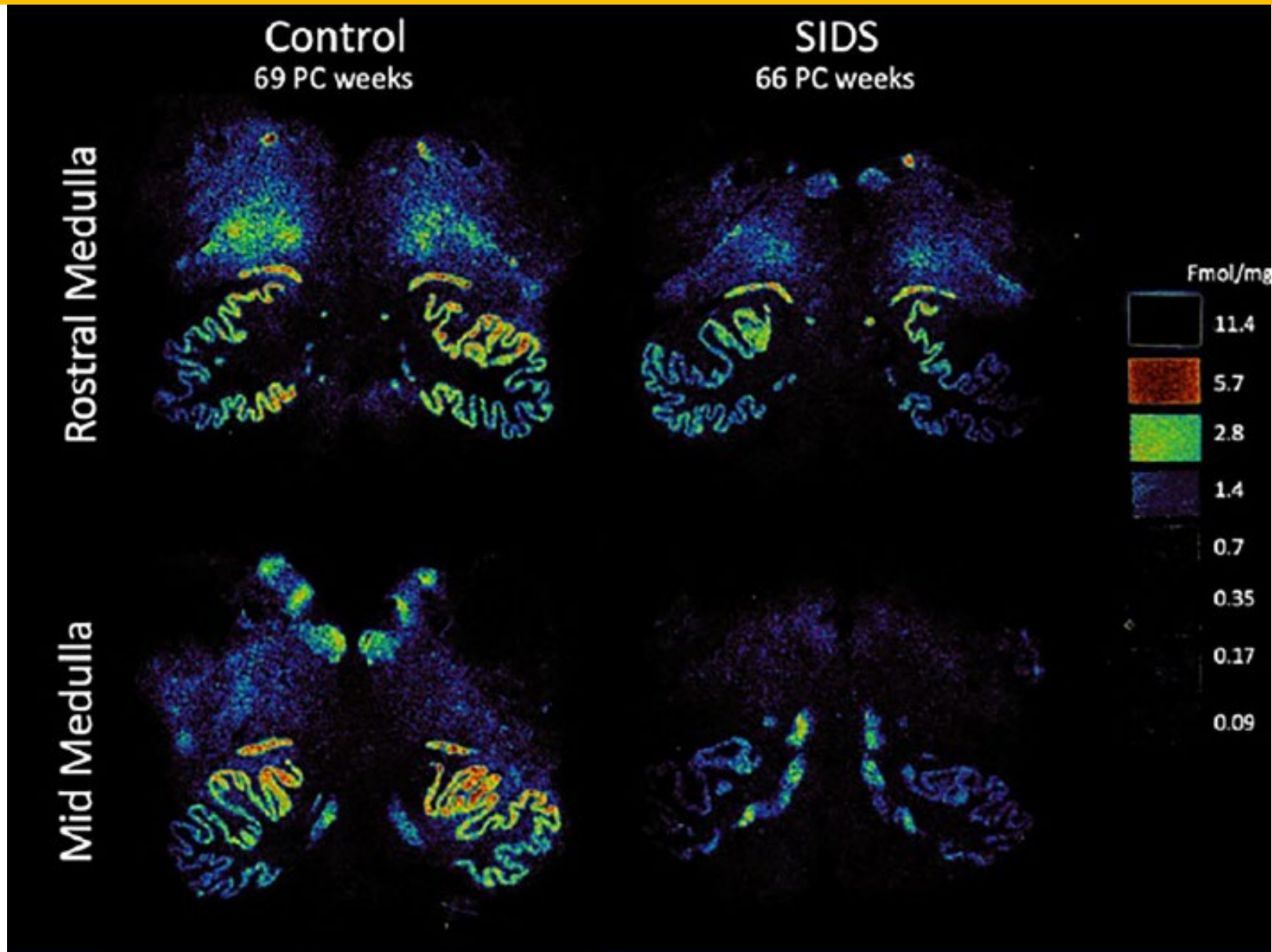
**C** Control Infant



Paterson, D.S., et al. *J. Amer. Med. Assoc.*, 296: 2124-2132, 2006.



# 5-HT<sub>1A</sub> Receptor Binding Density in SIDS Brainstems

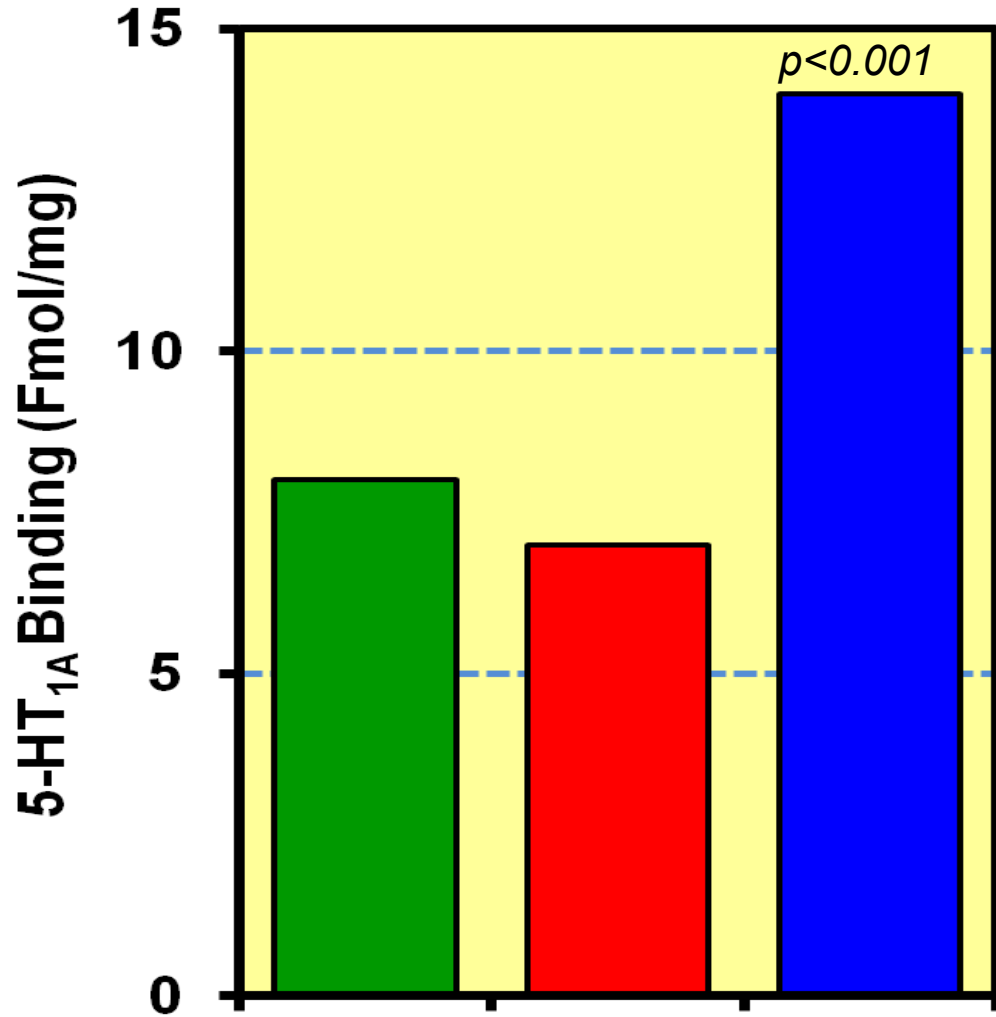


Haynes, R.L., et al. *J. Neuropathol., Exper. Neurol.*, doi.org/10.1093/jnen/nlad030, 2023.

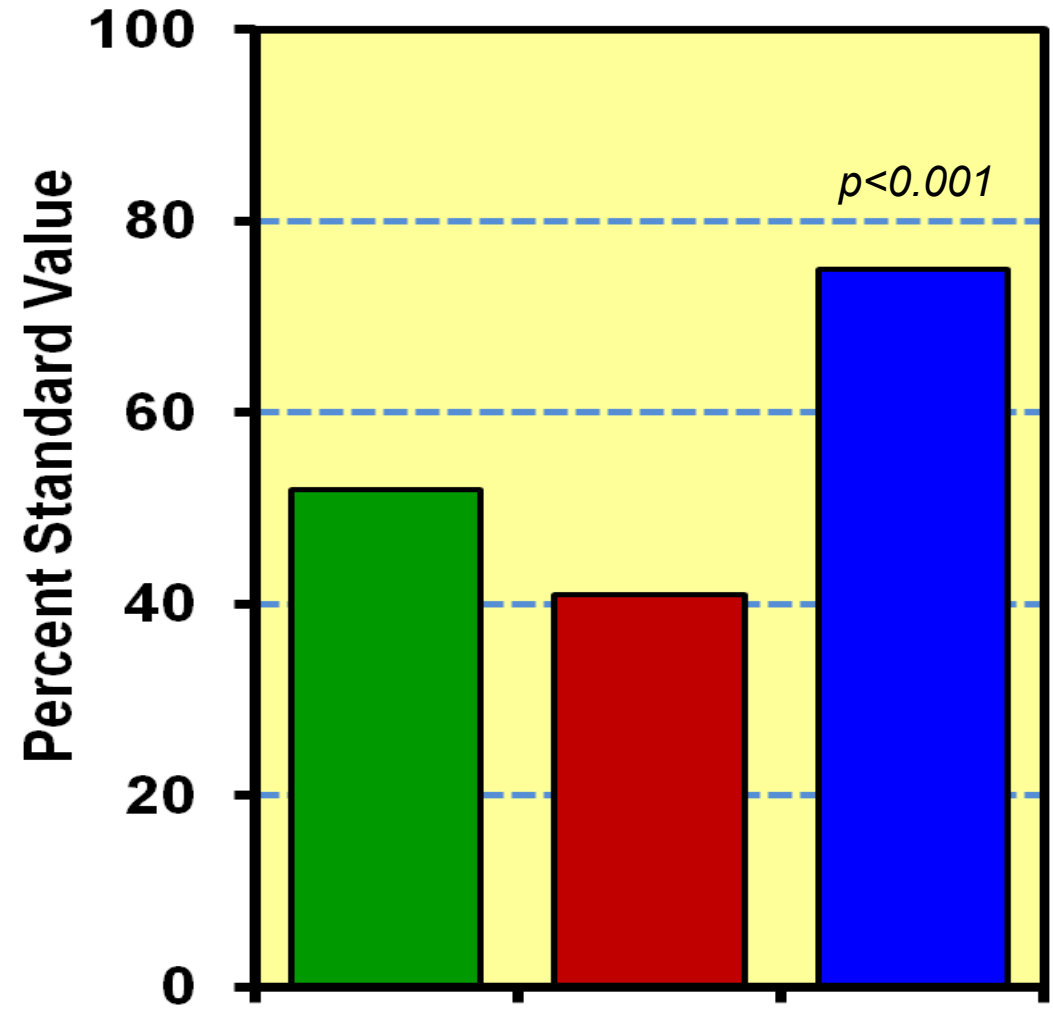


- Sudden death without Asphyxia
- Sudden death with Asphyxia
- Known Cause of Death

### Solitary Tract Nucleus



### Gigantocellularis





**Accidental  
Asphyxia or  
Suffocation**

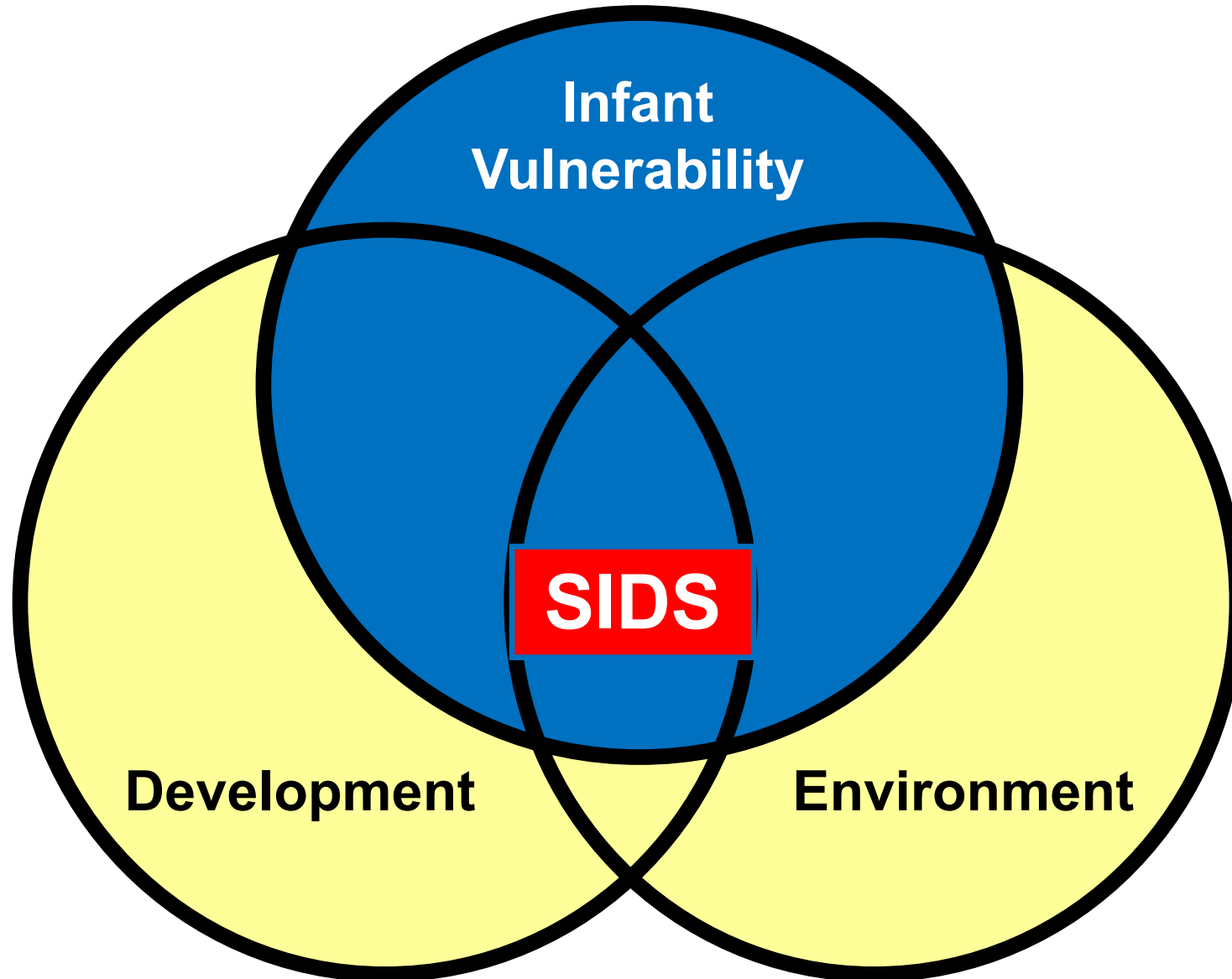
**Sudden  
Death with  
Asphyxia**

**Sudden Death  
without  
Asphyxia**



Randall, B.B., et al. *Pediatrics*, doi: 10.1542/peds.2013-0700. 2013.  
Goldstein, R.D., et al. *Pediatrics*, 137: e20154661, 2016.

# Infant Vulnerability may have Many Causes



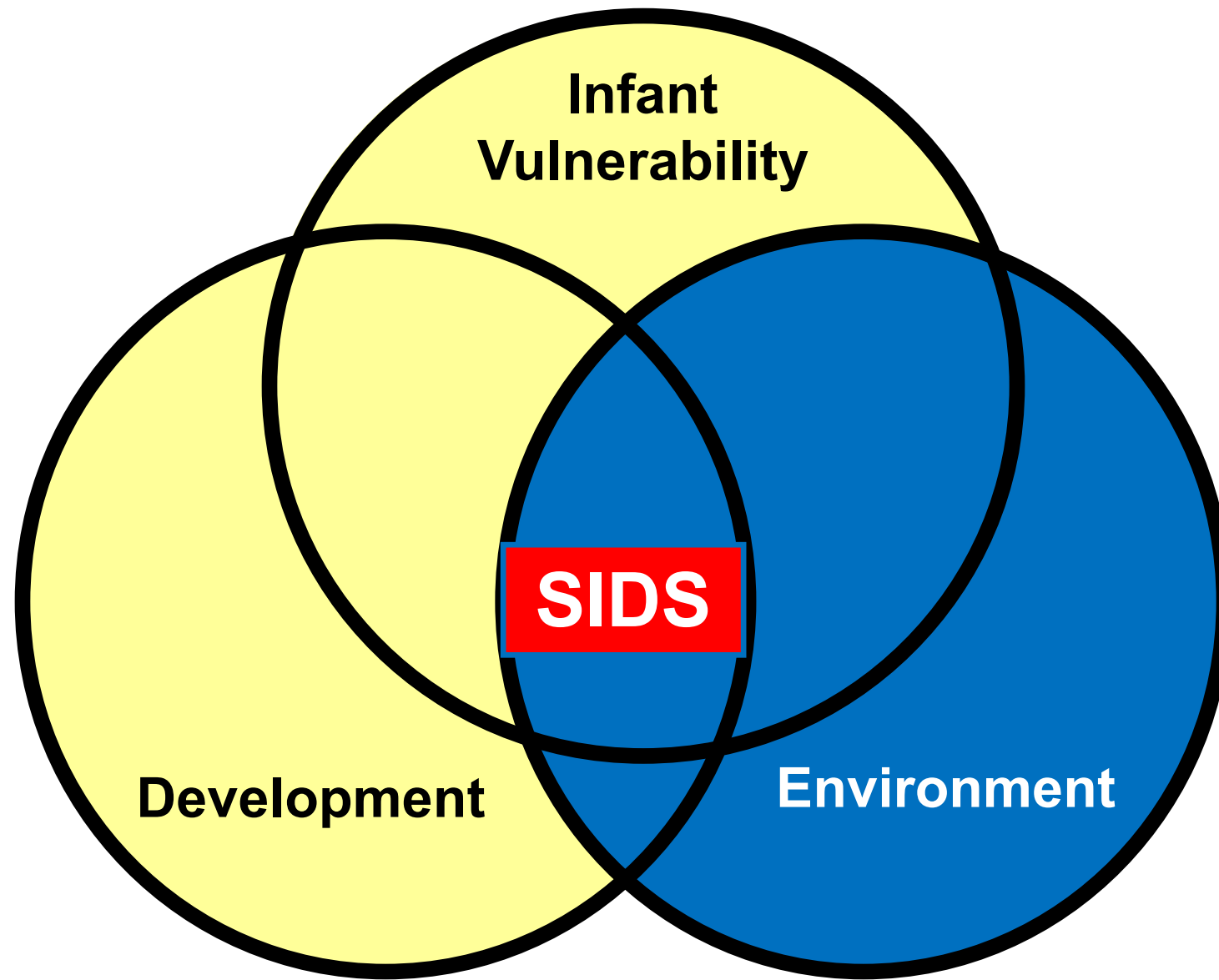
Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.

Imagine a car driving up a steep mountain road. The car has stopped. Why can't the car continue up the hill?

## A New Way of Thinking:

- Some cars are Ferrari's.
- Some cars are Jeep's.

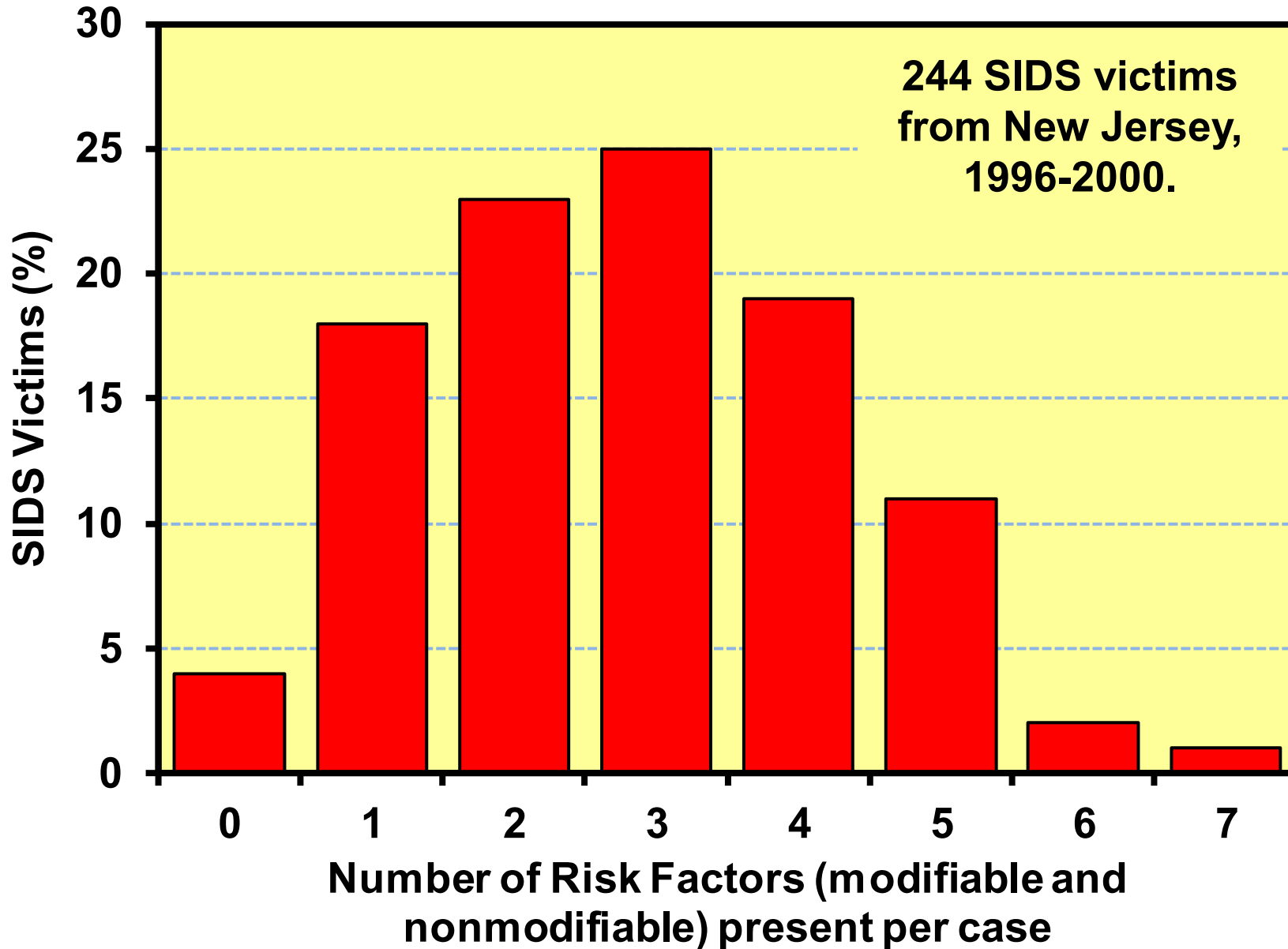




Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.



# The Majority of SIDS Victims Have $\geq 1$ Risk Factor



Ostfeld, B.M., et al. *Pediatrics*, 125: 447-453, 2010.



# How can we, as a population, reduce the risk of SIDS?



Keck School  
of Medicine  
of USC



Children's  
Hospital  
LOS ANGELES  
SUDDEN INFANT  
DEATH SYNDROME

USC University of  
Southern California

Children's  
Hospital  
LOS ANGELES  
DIVISION OF PEDIATRIC  
PULMONOLOGY AND  
SLEEP MEDICINE





# **Risk Factors $\neq$ Causes**

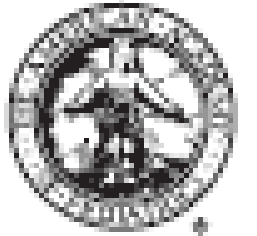
- **Most infants with risk factors will not die from SIDS.**
- **Some infants without risk factors will die from SIDS.**
- **However, infants with risk factors are at increased risk of dying from SIDS.**



## POLICY STATEMENT

Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

American Academy  
of Pediatrics



DEDICATED TO THE HEALTH OF ALL CHILDREN™

# Sleep-Related Infant Deaths: Updated 2022 Recommendations for Reducing Infant Deaths in the Sleep Environment

Rachel Y. Moon, MD, FAAP,<sup>a</sup> Rebecca F. Carlin, MD, FAAP,<sup>b</sup> Ivan Hand, MD, FAAP,<sup>c</sup>

THE TASK FORCE ON SUDDEN INFANT DEATH SYNDROME AND THE COMMITTEE ON FETUS AND NEWBORN

**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**

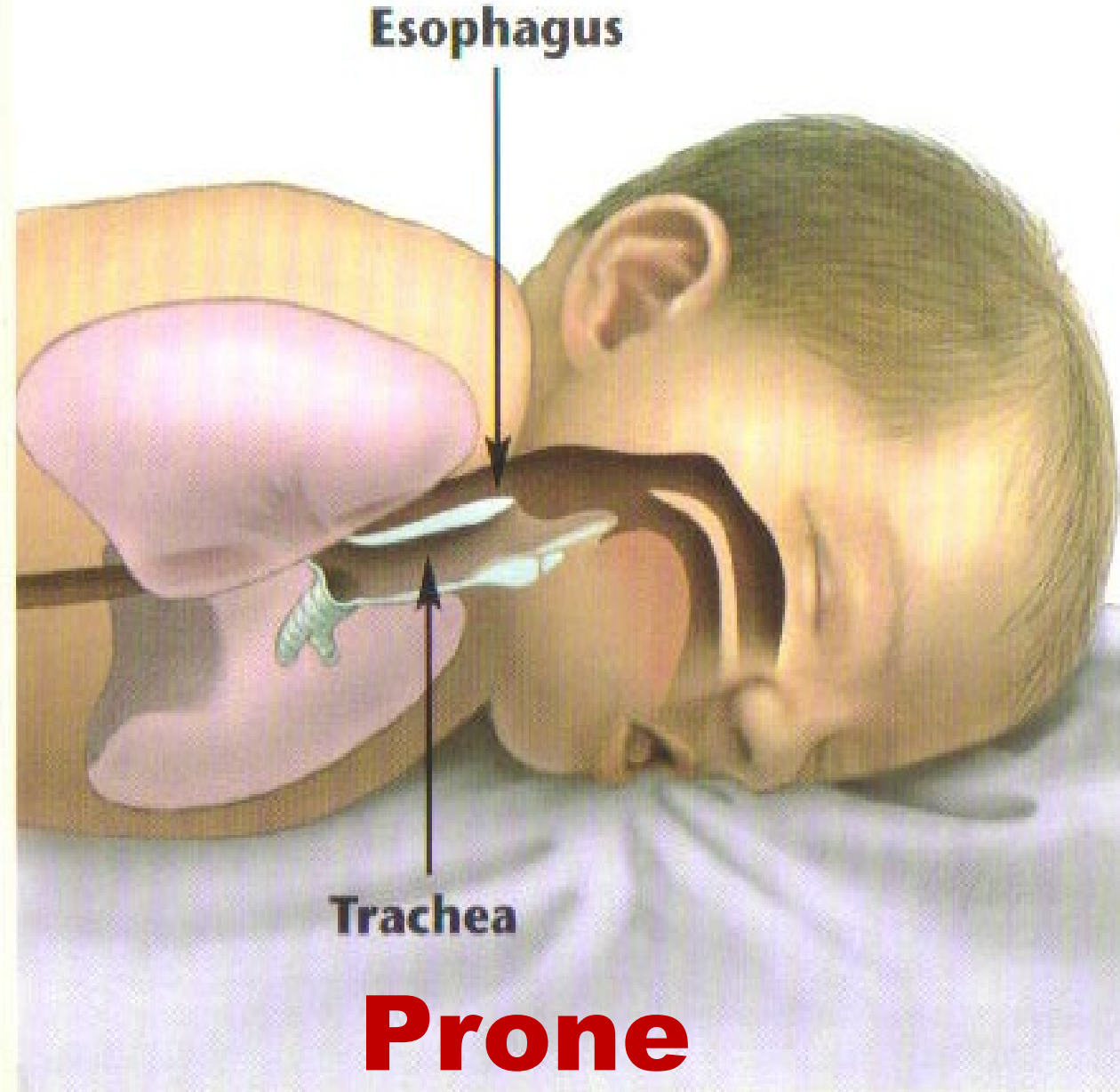
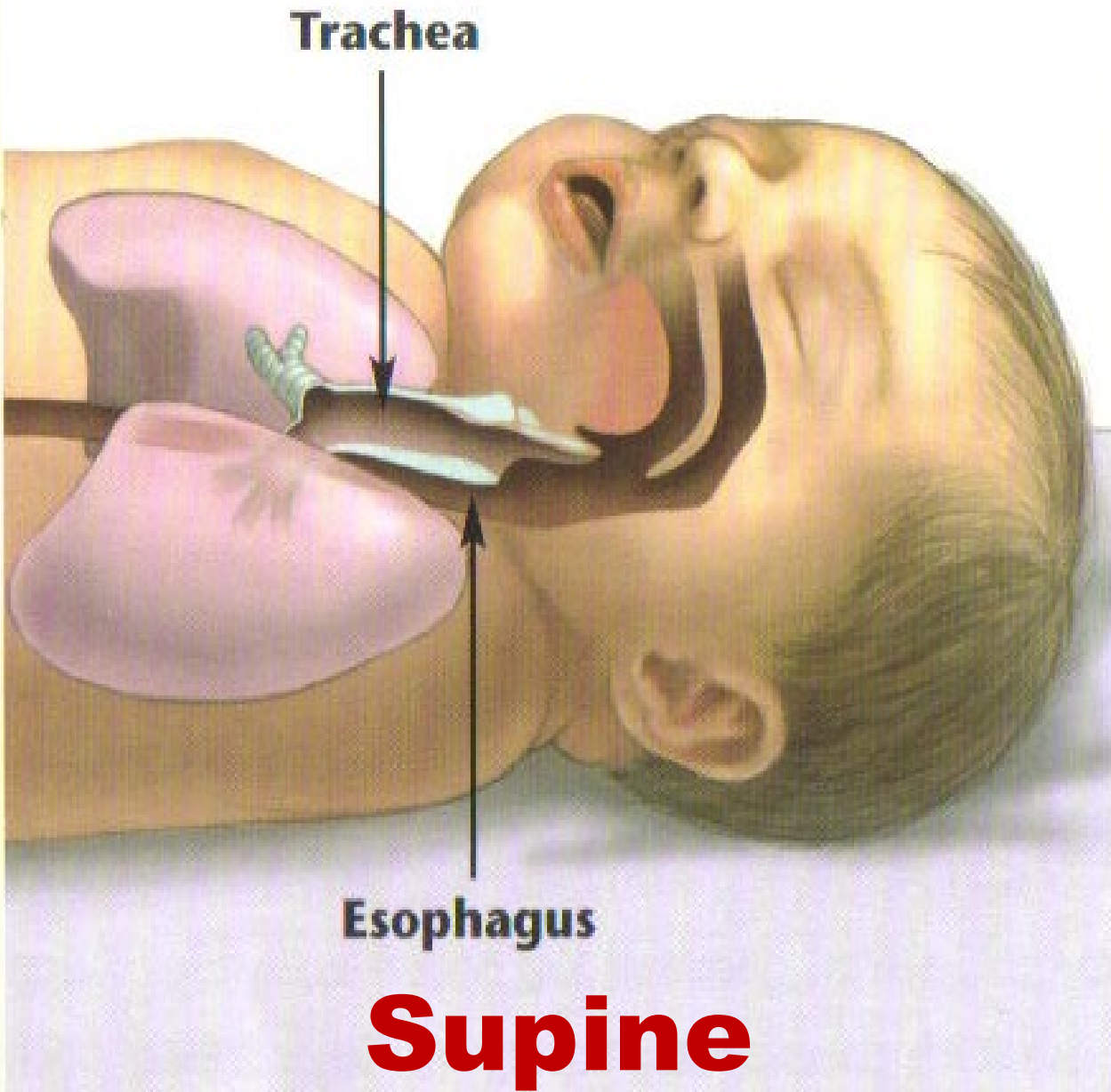


# Babies Should Sleep on their Backs for Every Sleep



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**

<http://www.medscape.com/features/slideshow/safe-sleep-principles?>







## New Emphasis in 2022:

- **Infants should sleep on a flat surface (<math><10^\circ</math> incline); including infants with GERD.**
- **Preterm infants should sleep supine as soon as medically stable; generally by 32-weeks PCA.**
- **Infants who roll may stay in their preferred position, but infant should be placed supine until 1-year of age.**
- **Skin-to-skin recommended at birth if the mother is alert, and if she is able to respond to her baby.**



# Use a Firm, Flat, Non-inclined Sleep Surface to Reduce the Risks of Suffocation, Wedging, and Entrapment



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



# Sitting Devices (Car Seats, Strollers, etc.) are Not Recommended for Routine Sleep



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**

<http://www.medscape.com/features/slideshow/safe-sleep-principles?>





# Feeding Human Milk is Recommended



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



# Roomsharing, Without Bedsharing, is Recommended



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**

<http://www.medscape.com/features/slideshow/safe-sleep-principles?>



## New Emphasis in 2022:

- **Couches, armchairs, and sofas are extremely dangerous.**
- **Inadvertent bedsharing may occur if a mother falls asleep while breastfeeding.**
- **Infants sleeping in a separate room from parents is associated with a 3-12 times increased risk of SIDS.**
- **Do not co-bed twins, triplets, etc.**





# Keep Soft Objects and Loose Bedding Out of the Crib



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**

<http://www.medscape.com/features/slideshow/safe-sleep-principles?>





# Consider Offering a Pacifier at Nap Time and at Bedtime



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**

<http://www.medscape.com/features/slideshow/safe-sleep-principles?>



# Avoid Cigarette Smoke Exposure and Vaping During Pregnancy and After Birth



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.





# Avoid Alcohol, Marijuana, and Illicit Drug Use During Pregnancy and After Birth



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



# Avoid Overheating and Head Covering; Infants Should Not Feel Hot to Touch



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**  
<http://www.medscape.com/features/slideshow/safe-sleep-principles?>



# Infants Should Be Immunized According to AAP and CDCP Advice



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**  
<http://healthlevelup.com/vaccinations-and-children/>



# Avoid Use of Commercial Devices Inconsistent with Safe Infant Sleep



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.





# Do Not Use Cardiorespiratory Monitors to Reduce the Risk of SIDS



Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



# Encourage *Tummy Time* when the Infant is Awake and Being Observed.



**Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.**  
<http://healthlevelup.com/vaccinations-and-children/>





# Avoid Swaddling if ...



- **Prone sleeping position.**
- **Thick blankets.**
- **Face covered.**
- **For infants older than 3-months.**  
**There is a danger when infants begin to roll from supine to prone, the swaddled infant can not regain the supine position.**

Ponsonby, A.L., et al. *N. Eng. J. Med.*, 329: 377-382, 1993.

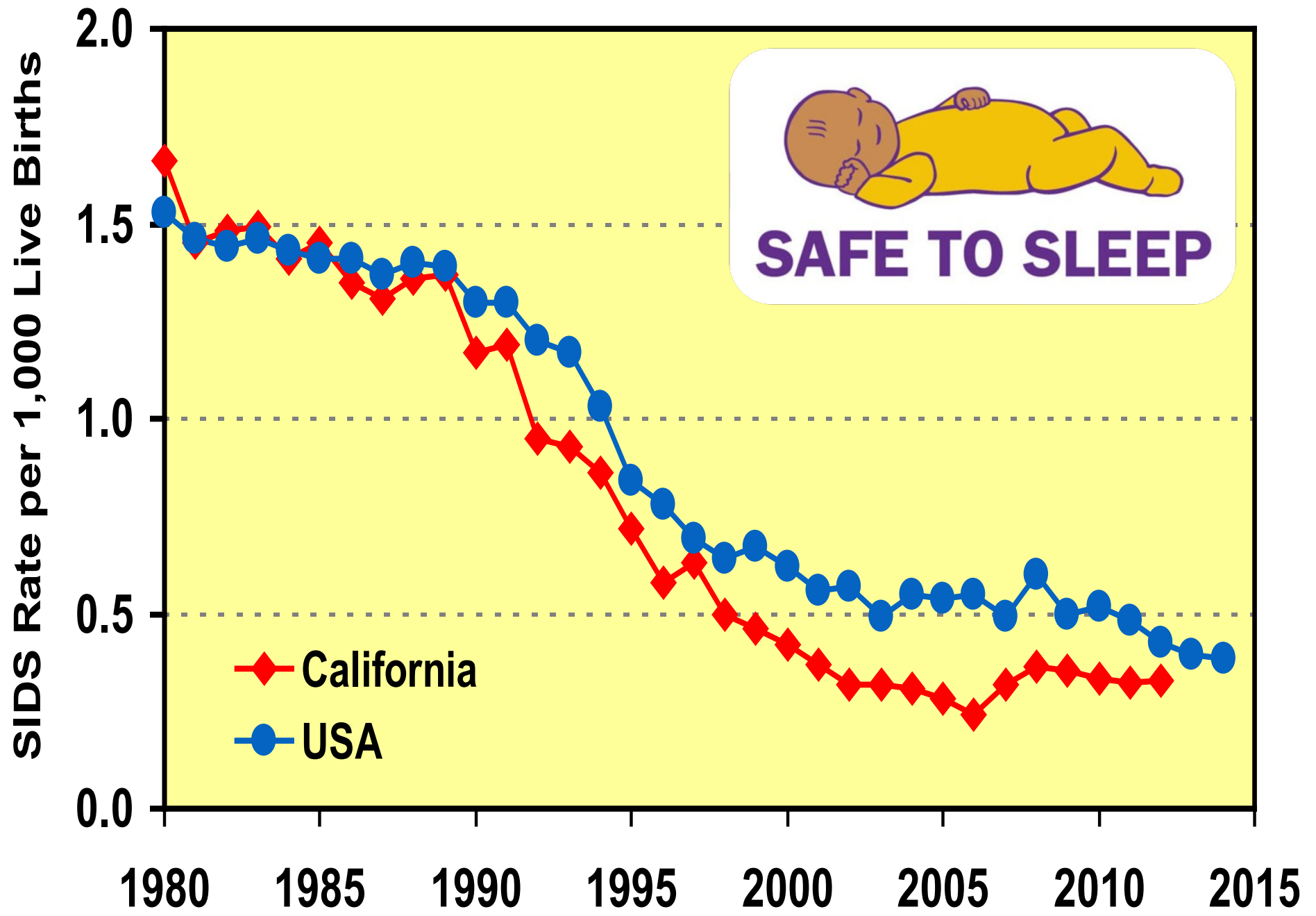
Wilson, C.A., et al. *J. Paed. Child Health*, 30: 506-512, 1994.

L'Hoir, M.P., et al. *Eur. J. Pediatr.*, 157: 681-688, 1998.

Van Sleuwen, B.E., et al. *Pediatrics*, 210: e1097-e1106, 2007.

Pease, A.S., et al. *Pediatrics*, 137: e20153275, 2016.

Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.





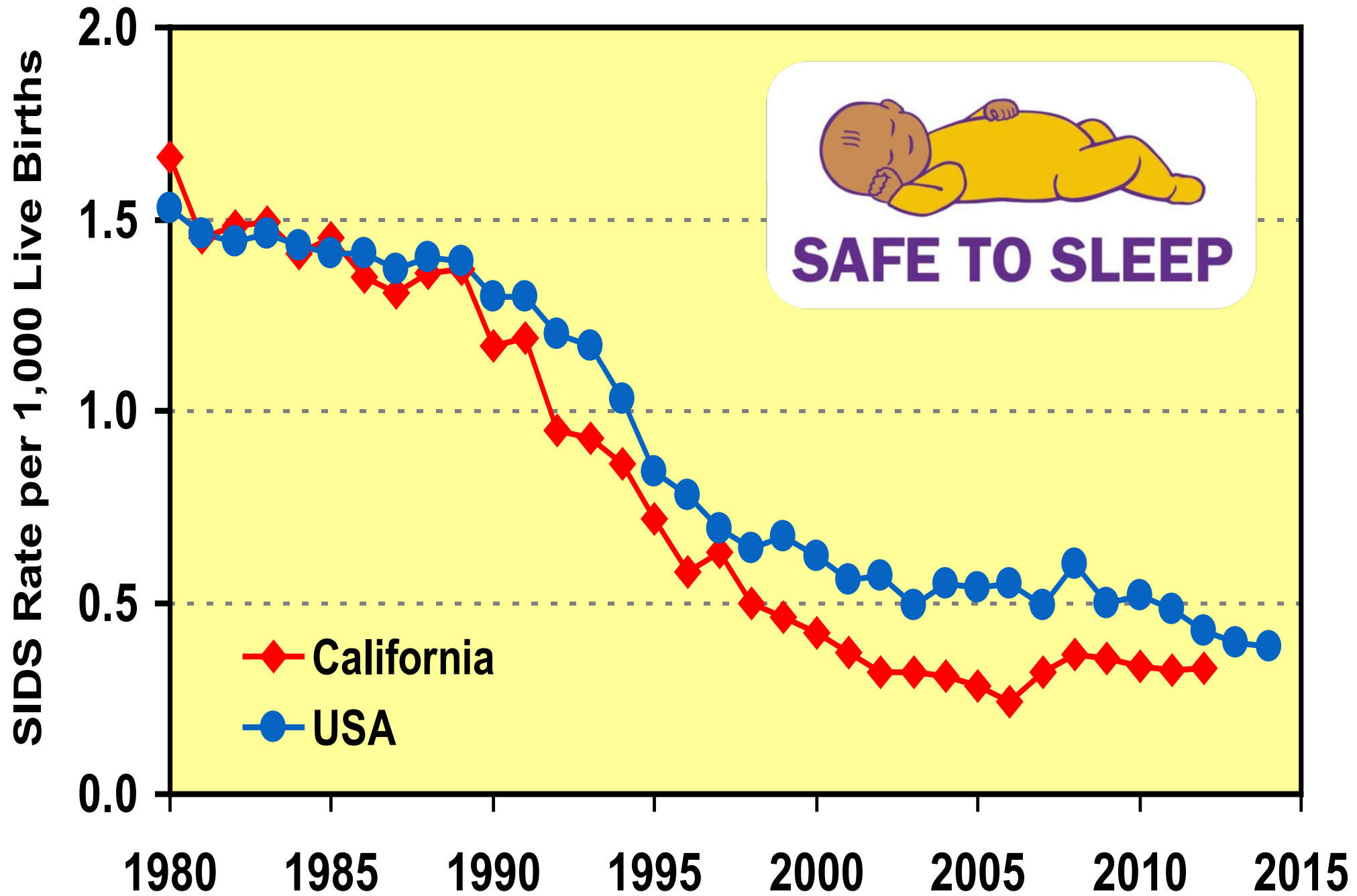
**S**upine

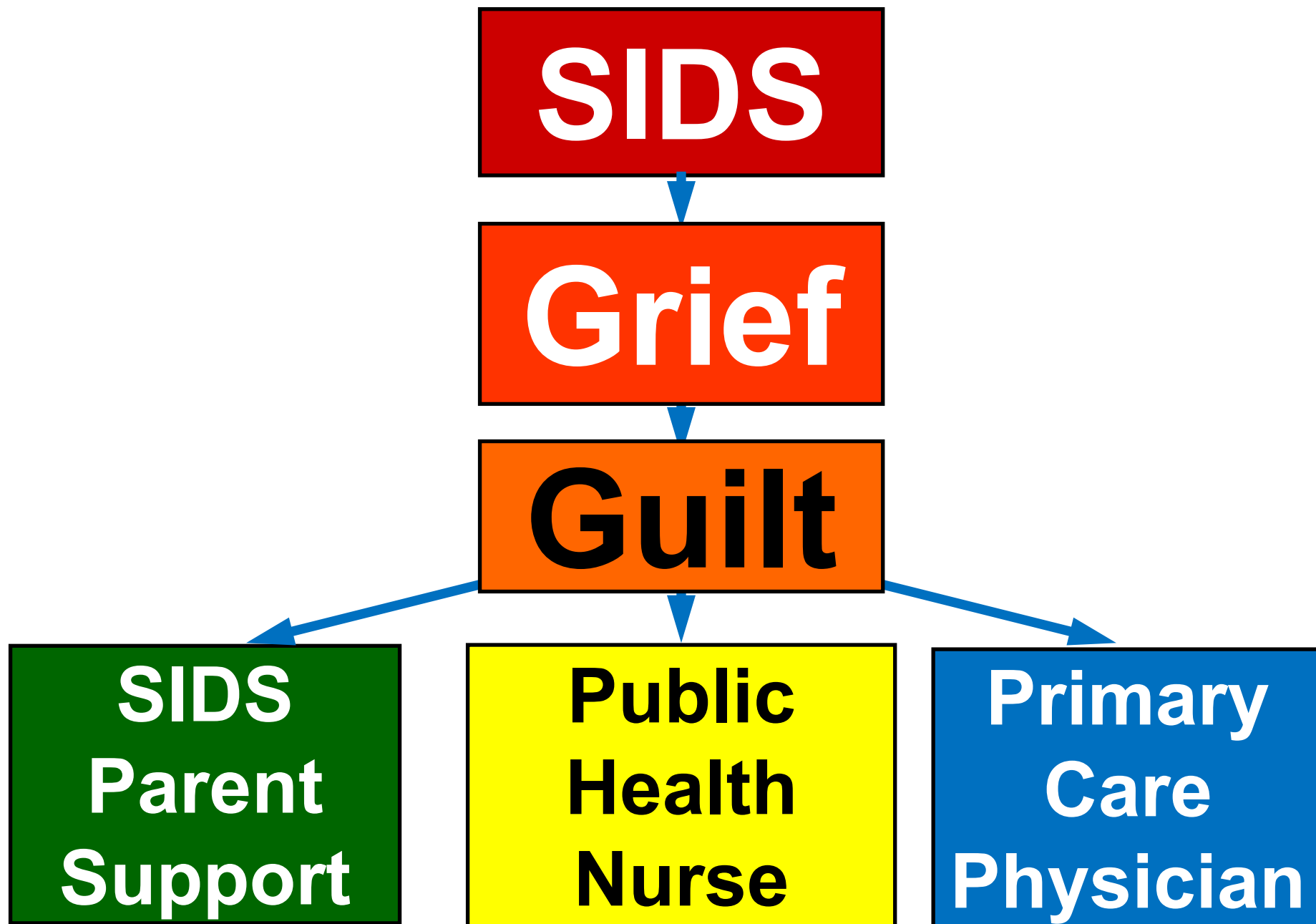
**A**lone

**F**irm mattress

**E**empty crib







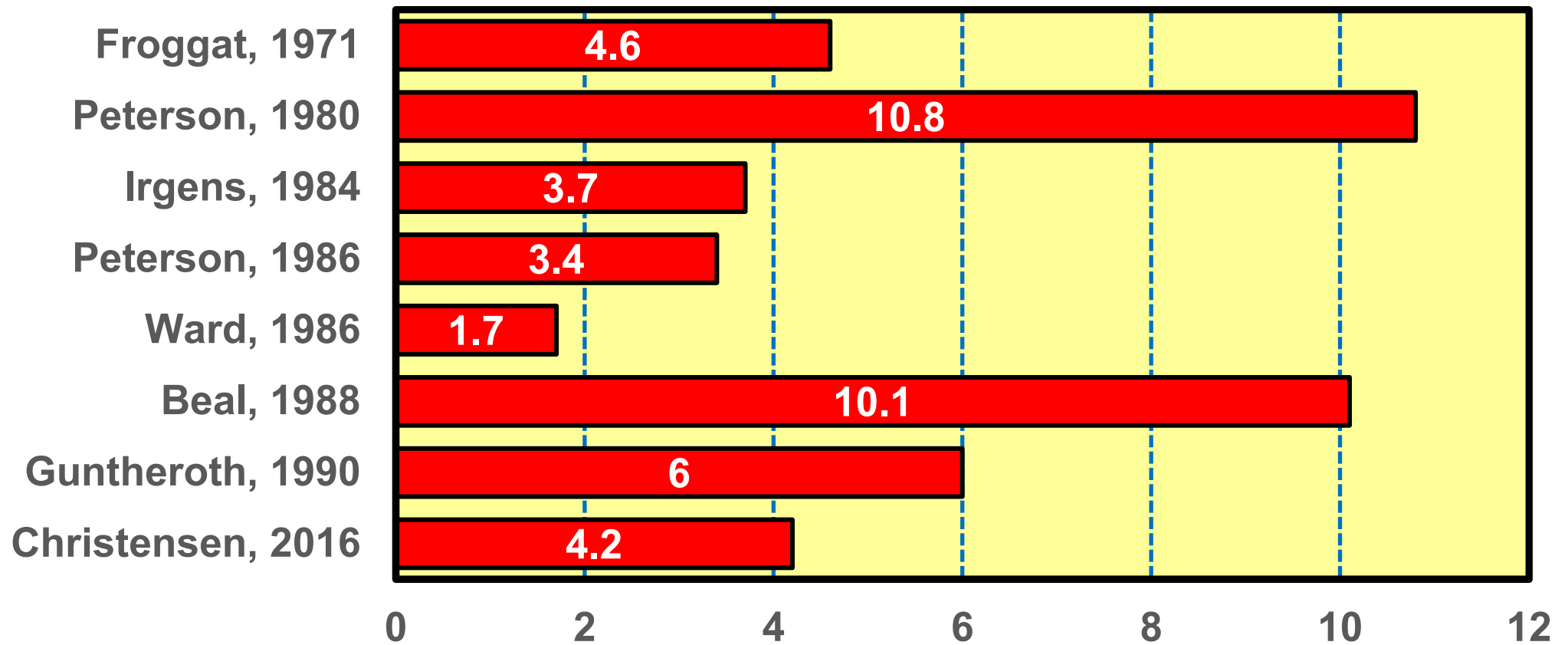
- **Meet with the parents.**
- **Refer them to a SIDS Parent Support group.**
- **As an authority on healthcare, tell them:**
  - **There is nothing they did to cause the death.**
  - **There is nothing they could have done to prevent the death.**
- **Recognize that health care professionals also feel guilty.**



# Are Subsequent Siblings of SIDS Victims at Increased Risk for SIDS?



- **SIDS is not hereditary.**
- **SIDS victims have a higher proportion of gene variants that may be associated with sudden death.**
- **Investigators do not think these caused death, but could they increase an infant's vulnerability?**
- **Conventional wisdom is that subsequent siblings of SIDS are not at increased risk of dying from SIDS.**



**SIDS Siblings Odds Ratio for SIDS compared to No SIDS in Family**

Froggat, P., et al. *Br. J. Prev. Soc. Med.*, 25: 119-134, 1971.

Peteron D.R., et al. *J. Pediatr.*, 97: 263-267. 1980.

Irgens, L.M., et al. *J. Pediatr.*, 104: 349-351, 1984.

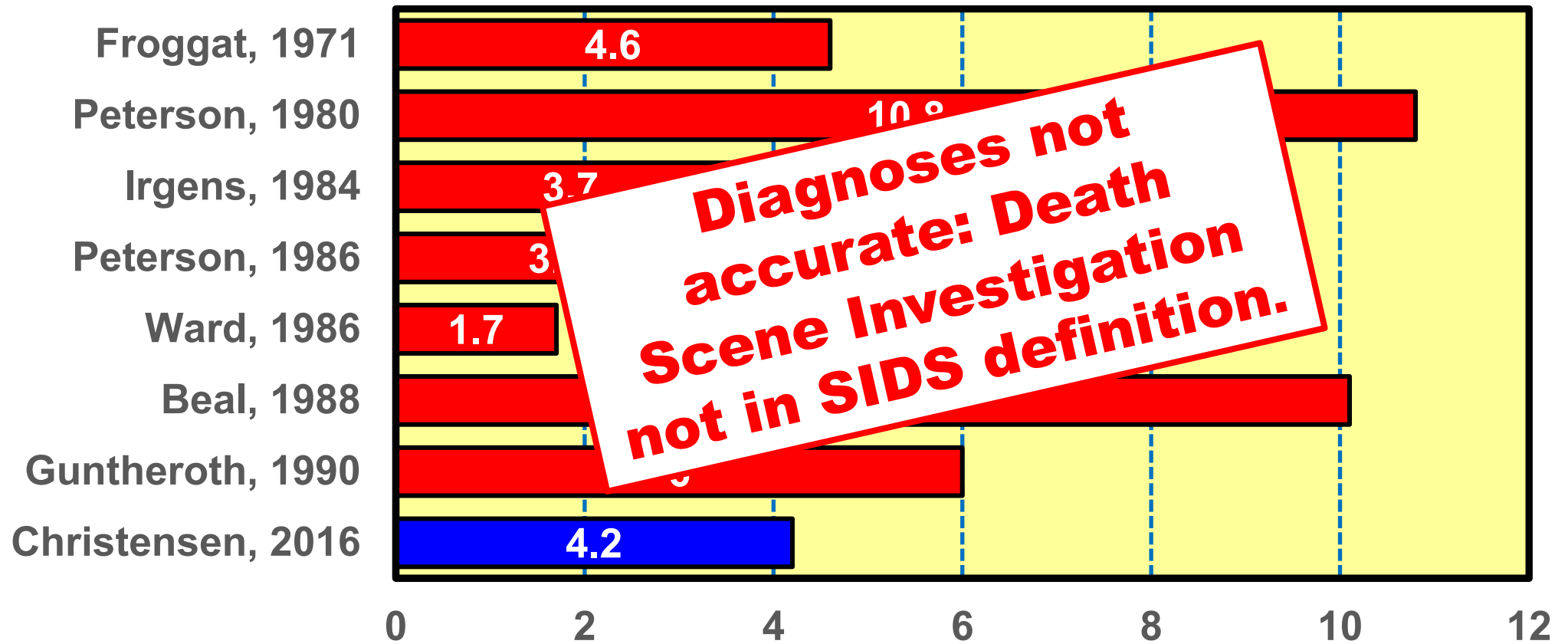
Peterson, D.R., et al. *J. Pediatr.*, 108: 911-914, 1986.

Ward, S.L.D., et al. *Pediatrics*, 77: 451-455, 1986.

Beal, S. *Arch. Dis. Child.*, 63: 924-930, 1988.

Guntheroth, W.G., et al. *J. Pediatr.*, 116: 520-524, 1990.

Christensen, E.D., et al. *Amer. J. Med. Genet. Part A*, 173A: 177-182, 2017.



**SIDS Siblings Odds Ratio for SIDS compared to No SIDS in Family**

Froggat, P., et al. *Br. J. Prev. Soc. Med.*, 25: 119-134, 1971.  
 Peteron D.R., et al. *J. Pediatr.*, 97: 263-267. 1980.  
 Irgens, L.M., et al. *J. Pediatr.*, 104: 349-351, 1984.  
 Peterson, D.R., et al. *J. Pediatr.*, 108: 911-914, 1986.  
 Ward, S.L.D., et al. *Pediatrics*, 77: 451-455, 1986.  
 Beal, S. *Arch. Dis. Child.*, 63: 924-930, 1988.  
 Guntheroth, W.G., et al. *J. Pediatr.*, 116: 520-524, 1990.  
 Christensen, E.D., et al. *Amer. J. Med. Genet. Part A*, 173A: 177-182, 2017.

- **Many of these studies had few SIDS; 2-18.**
- **Diagnoses not precise in all studies, except about half of those in Christensen et al.**
- **Some studies show death rates similar to siblings of children who died from other causes.**

Froggat, P., et al. *Br. J. Prev. Soc. Med.*, 25: 119-134, 1971.

Peteron D.R., et al. *J. Pediatr.*, 97: 263-267, 1980.

Irgens, L.M., et al. *J. Pediatr.*, 104: 349-351, 1984.

Peterson, D.R., et al. *J. Pediatr.*, 108: 911-914, 1986.

Ward, S.L.D., et al. *Pediatrics*, 77: 451-455, 1986.

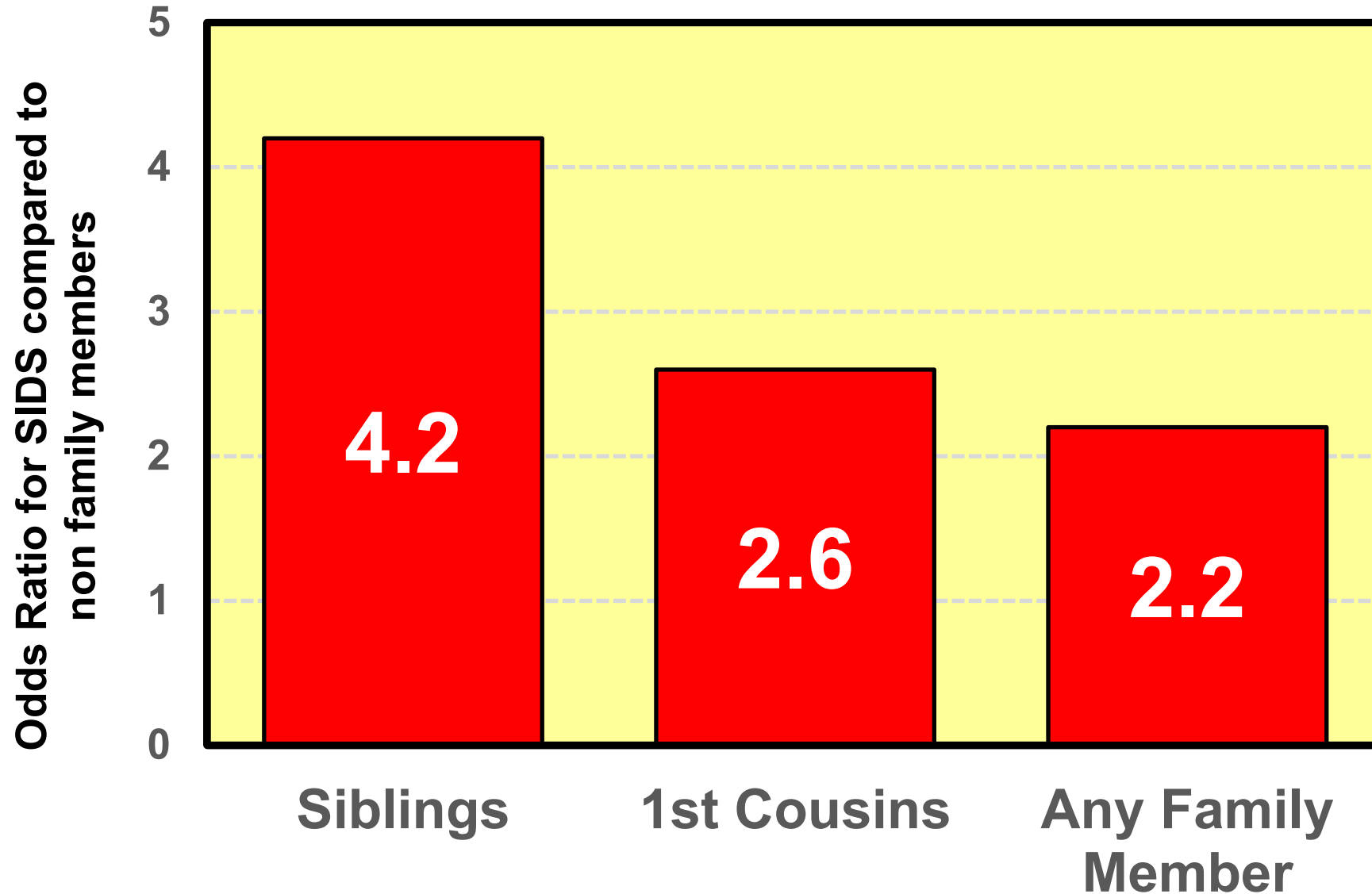
Beal, S. *Arch. Dis. Child.*, 63: 924-930, 1988.

Guntheroth, W.G., et al. *J. Pediatr.*, 116: 520-524, 1990.

Christensen, E.D., et al. *Amer. J. Med. Genet. Part A*, 173A: 177-182, 2017.



# Subsequent Siblings of SIDS Victims



- **Not clear if subsequent siblings of SIDS victims actually are at increased risk of recurrent SIDS.**
- **Parents of subsequent siblings of SIDS are more likely to adhere to safe infant sleep, perhaps reducing their risk.**
- **Even if risk is increased, recurrent SIDS is a rare event.**
- **This may not be reassuring to a family who already experienced a SIDS death.**

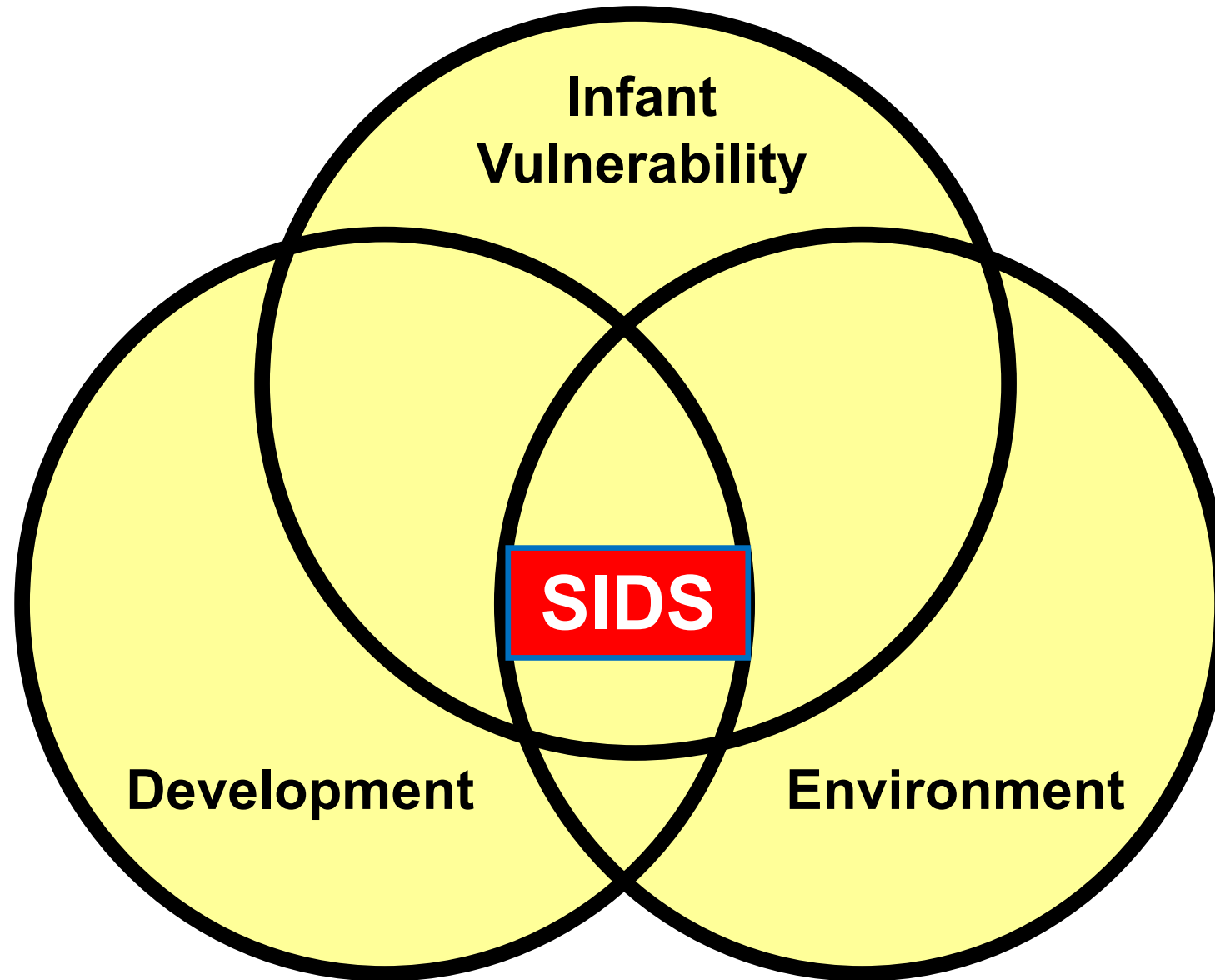
Ramanathan, R., et al. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.

Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.

- **No specific diagnostic tests or interventions are required.**
- **Home infant apnea-bradycardia monitors, used for over a decade, did not decrease the SIDS rate.**
- **Should adhere to Safe to Sleep recommendations, which is the only evidence-based strategy to reduce the risk of SIDS.**

Ramanathan, R., et al. *J. Amer. Med. Assoc.*, 285: 2199-2207, 2001.

Moon R.Y., et al. *Pediatrics*, 150: e2022057990, 2022.



Filiano, J.J., and H.C. Kinney. *Biol. Neonate*, 65: 194-197, 1994.

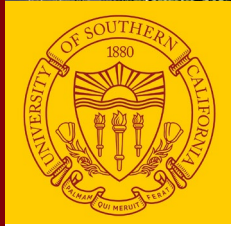


- **Most common cause of sudden infant death between the ages of 1-month and 1-year.**
- **Cause remains unknown.**
- **Can not be predicted in infants prior to death.**
- **Reduction in SIDS in populations through public health intervention.**
- **SIDS has not been eliminated.**





Keck School  
of Medicine  
of USC



Children's  
Hospital  
LOS ANGELES  
SUDDEN INFANT  
DEATH SYNDROME

USC University of  
Southern California

Children's  
Hospital  
LOS ANGELES  
DIVISION OF PEDIATRIC  
PULMONOLOGY AND  
SLEEP MEDICINE

