Published in final edited form as:

Pediatrics. 2009 November ; 124(5): e1001–e1006. doi:10.1542/peds.2008-3233.

SNAP-II and SNAPPE-II as predictors of death among infants born before the 28th week of gestation. Inter-institutional variations

Olaf Dammann, MD, SM^{1,2,3,*}, Bhavesh Shah, MD^{4,*}, Mary Naples, RN, BSN, CAS^{5,**}, Francis Bednarek, MD^{5,**}, John Zupancic, MD, ScD^{6,7}, Elizabeth N. Allred, SM^{3,7,8}, and Alan Leviton, MD, SM^{3,7} for the ELGAN Study Investigators

¹Newborn Medicine, Floating Hospital for Children at Tufts Medical Center, Boston MA

²Perinatal ID Epidemiology Unit, Hannover Med School, Germany

³Neuroepidemiology Unit, Children's Hospital, Boston MA

⁴Div. of Neonatology, Baystate Med Center, Springfield MA

⁵Div. of Neonatology, U Mass Memorial Health Care, Worcester MA

⁶Beth Israel Deaconess Medical Center, Boston MA

⁷Harvard Medical School, Boston MA

⁸Harvard School of Public Health, Boston MA

Abstract

Background—Illness severity scores predict death among infants admitted to neonatal intensive care units. We know of no study limited to a population defined by an extremely low gestational age.

Methods—A total of 1467 infants born before the 28th postmenstrual week at 14 institutions were given Scores for Neonatal Acute Physiology (SNAP-II and SNAPPE-II) based on data collected within the first 12 postnatal hours. All deaths in the intensive care nursery were identified.

Results—The mortality rate before postnatal day 28 was 13% (inter-institutional range: 7–20%), while the overall mortality was 18% (8–31%). SNAP-IIs, SNAPPE-IIs, and death rates tended to decrease with increasing gestational age. However, even within gestational age strata, the risk of death declined with decreasing SNAP-IIs and SNAPPE-IIs. The predictive value positive of most SNAP-II and SNAPPE-II cut-offs was close to 30. In general an institution's death rate increased with the proportion of infants whose SNAP-II was 30 or more.

Conclusion—The physiologic instability in the first 12 post-natal hours identified by illness severity scores conveys information about the risk of death among infants at the lowest gestational ages.

Keywords

Newborn; preterm; illness severity; mortality prediction; risk assessment

Corresponding author: Olaf Dammann, Floating Hospital for Children at Tufts Medical Center, Box 854, 800 Washington St., Boston, MA 02111, USA T (617) 636 0240, F (617) 636 8943, odammann@tuftsmedicalcenter.org.

*These two authors contributed equally

**These two authors contributed equally

Financial disclosures and conflicts of interest: Dr. Zupancic is employed by the Beth Israel Deaconess Medical Center, which, along with the University of British Columbia and Kaiser Permanente Health Care Systems, holds the patent for the revised Score for Neonatal Acute Physiology.

Introduction

Comparing the mortality rates of neonatal intensive care units (NICUs) without adjusting for the severity of illness of the newborns admitted to each NICU can obscure differences in care that might influence the mortality rate. Illness severity scores, such as the Score for Neonatal Acute Physiology (SNAP) have been used to adjust for these institutional differences ¹.

The 16 components of the original SNAP were reduced to 6 to create the easier-to-use SNAP-II, and supplemented with information about birth weight, intrauterine growth restriction and Apgar score at 5 minutes to create SNAPPE-II ². Their usefulness was recently re-emphasized in the Vermont-Oxford Network database ³.

SNAP-II was intended for use at all gestational ages. A high (ominous) score conveys death-risk information about a term newborn, whose peers have much lower scores. Does a high score in an infant born much before term, many of whose peers also have scores not much more favorable, convey as much information as a high score in a term-born infant? Several studies of very low birth weight newborns have produced varying results ^{3–6}. We know of no study that has evaluated SNAP-II or SNAPPE-II among extremely low gestational age newborns.

Our large prospective cohort study of infants born before the 28th week provided us the opportunity to see how well SNAP-II and SNAPPE-II predict death in this sample of newborns at very high risk of death. It also allowed us to see how the additional consideration of information about gestational age might further improve prediction of death.

Methods

The ELGAN study was designed to identify characteristics and exposures that increase the risk of structural and functional neurologic disorders in ELGANs (the acronym for Extremely Low Gestational Age Newborns). During the years 2002–2004, women delivering before 28 weeks gestation at one of 14 participating institutions in 11 cities in 5 states were invited to participate in the study. The enrollment and consent processes were approved by the individual institutional review boards.

Mothers were approached for consent either upon antenatal admission or shortly after delivery, depending on clinical circumstance and institutional preference. 1249 mothers of 1506 infants consented. Approximately 260 additional eligible women were either missed or did not consent to participate. We excluded 39 of the enrolled ELGANs who did not have all components for calculating a SNAP-II ². The remaining 1467 inborn infants constitute the sample for this study.

Each of the participating neonatal intensive care units (NICUs) is part of a teaching hospital. During the approximately 16 months of enrollment and data collection, each NICU contributed between 29 and 193 subjects to this study.

Newborn variables

Data were collected by research nurses trained specifically for the ELGAN study. The gestational age estimates were based on a hierarchy of the quality of available information. Most desirable were estimates based on the dates of embryo retrieval or intrauterine insemination or fetal ultrasound before the 14th week (62%). When these were not available, reliance was placed sequentially on a fetal ultrasound at 14 or more weeks (29%), last menstrual period without fetal ultrasound (7%), and gestational age recorded in the log of the neonatal intensive care unit (1%).

We collected all the physiology, laboratory and therapy data for the first 12 hours needed to calculate a SNAP-II™ score². We also collected the date of death, transfer or discharge. Mortality was considered as both neonatal (within first 28 days) and total mortality (to transfer or discharge).

Data analysis

We evaluated the following generalized null hypotheses:

1. Distributions of SNAP-II and SNAPPE-II do not vary among gestational age groups.
2. Mortality does not vary with the distribution of SNAP-II or SNAPPE-II.
3. Adjusting for gestational age does not influence the ability of SNAP-II or SNAPPE-II to predict death.

Assessing SNAP-II and SNAPPE-II as continua has limitations, primarily because the risk of dying might not vary linearly with SNAP-II and SNAPPE-II. Consequently, we explored dichotomies we expected might be useful. Because we did not know what dichotomy might be best for each prediction, we explored a variety of dichotomies (*e.g.*, arbitrary cutoffs, highest decile for gestational age, highest quartile for gestational age, Z-score > 1) for each of the outcomes of interest. Several of these cutoffs are within gestational age groups because we were concerned that adjusting for gestational age might not eliminate all of the gestational age related information about mortality conveyed by SNAP-II and SNAPPE-II.

Because SNAP-II varies with gestational age (Figure 1), we explored how best to utilize the risk information provided by gestational age. In early sets of analyses, we adjusted for gestational age in two ways, by both week of gestation (23, 24, 25, 26, 27), and by groups of weeks (23–24, 25–26, 27). Each provided almost identical results. Here we present data adjusted for gestational age in groups of weeks.

Members of the Vermont Oxford Network (VON) SNAP Pilot Project graciously provided the median and standard deviation of SNAP-II and SNAPPE-II for each week of gestation³. This allowed us to create a SNAP-II Z score and a SNAPPE-II score for each newborn in our study.

The SNAP-II-Z score is the difference between the observed SNAP-II and the median SNAP-II for the same gestational age in the referent VON sample divided by the standard deviation of the SNAP-II at that gestational age. Because they incorporate the standard deviation, Z scores provide information about SNAP-II variability at each gestational age. They are in units of standard deviations from the gestational-age-specific median and follow a Gaussian distribution with a median of 0 and a variance of 1.

We calculated predictive values positive and negative of death within the first postnatal month for each SNAP-II and SNAPPE-II cut-off⁷. We also summarize some of our data with box and whiskers plots of the central tendency and scatter of SNAP-IIs at each week of gestational age separately among those who died and those who survived (Figure 1). These displays provide a quick sense of how skewed are the data.

Results

The only component of the SNAP-II that did not seem to apply to infants in our extremely low gestational age sample was the query about seizures. No infant in our sample had multiple clinically-evident seizures.

SNAPs and gestational age

The median SNAP-II, as well as the 25th and 75th centiles decreased progressively with increasing gestational age between 23 weeks and 26 weeks, when it appears to have leveled off (Figure 1).

SNAPs, mortality, and adjustment for gestational age

At every week of gestation, those who subsequently died had a higher SNAP-II (Figure 1) and SNAPPE-II (not shown) than those who survived. The narrower range of SNAPs among children who survived than among those who died is expected in light of the often more than 4-fold greater number of survivors.

We arbitrarily defined a SNAP-II value of 30 or more as “high,” thereby identifying the 28% of our sample at highest risk of dying. Our SNAPPE-II cut off of 45 identified the top 32%. Without adjusting for gestational age, infants with a SNAP-II of 30 or more were almost 6 times more likely to die than infants who had a lower SNAP-II, whereas infants whose SNAPPE-II was 45 or higher were almost 7 times more likely to die than infants with a lower SNAPPE-II (Table 1). Adjusting both SNAP-II and SNAPPE-II for gestational age reduced the odds of dying to 3.5 for a SNAP-II ≥ 30 and 3.9 for SNAPPE-II ≥ 45 .

When cut-offs were based on the range for each child's gestational age at birth, SNAPPE-II provided minimally to modestly higher point estimates of dying than SNAP-II. For example, a SNAP-II in the highest quartile for gestational age and adjusted for gestational age had an odds of death of 2.6, whereas a SNAPPE-II in the highest quartile for gestational age and adjusted for gestational age had an odds of death of 3.0. The differences were even smaller for the highest deciles for gestational age. In contrast, a SNAPPE-II Z-score of greater than 1.0 (indicating more than one standard deviation above the median for gestational age) had a higher odds ratio of death than the equivalent SNAP-II Z-score (4.4 vs 3.0).

Predictive values positive and negative for death within the first postnatal month

The highest quartile for gestational age cut-off has the lowest predictive value positive for both SNAP-II and SNAPPE-II, close to 20, which means that approximately one of five children with such a high SNAP will die before the end of the first postnatal month. The other 3 cut-offs have predictive values positive close to 30. All of the cut-offs have predictive values negative of at least 89 (Table 1).

Inter-institutional differences

The distributions of gestational age at birth varied at the participating NICUs. For example, the proportion of all infants born at 23–24 weeks varied from a low of 7% to a high of 39%, while the proportion of all infants born at 27 gestational weeks ranged from 17% to 49%. The NICUs also varied in the distribution of SNAP-IIs of the infants enrolled in this study. As might be expected, a tendency was seen for the NICUs with the higher percents of infants born at 27 weeks to have the lower SNAPs.

The mortality rate before postnatal day 28 was 13% and ranged among participating institutions from a low of 7% to a high of 20%. A total of 18% of infants admitted to the intensive care nursery died before discharge (institutional range: 8–31%). The relationship between SNAP-II and mortality was very similar for death before day 28 and for death before discharge. In general, the higher the proportion of infants with a SNAP-II score of 30 or more at an institution, the higher the neonatal and total mortality rates (data not shown).

Institutions with a high proportion of babies who had a SNAP-II of 30 or higher did not tend to have median values of any SNAP-II component that were different from those of institutions with lower proportions of babies who had a high SNAP-II (Table 3).

Discussion

Our major finding is that SNAP-II and SNAPPE-II predict death at the population level, not at the individual level, among infants born at extremely low gestational ages, even after adjusting for gestational age. Thus, illness-severity scores intended to predict death among the whole range of newborns admitted to an intensive care nursery appear to be applicable to the narrow gestational age range of 23–27 weeks.

SNAPs and gestational age

Because the SNAP-II distributions were not normally distributed, we have avoided means and standard deviations and have instead emphasized centiles of the distribution. The median (50th centile) SNAP-II, as well as the 25th and 75th centiles decreased progressively with increasing gestational age between 23 weeks and 26 weeks, when it appears to have leveled off (Figure 1). This, as well as the sharp reduction in odds of dying when SNAP-II and SNAPPE-II are adjusted for gestational age, allows for the inference that SNAP-IIs and SNAPPE-IIs provide information about gestational age, and that they can function, in part, as surrogates for gestational age.

When adjustment is made for gestational age, the odds ratios for the arbitrary cutoffs of SNAP-II and SNAPPE-II are reduced. This indicates that the odds ratios were confounded by gestational age. In contrast, the odds ratios for the gestational-age-defined SNAP-II and SNAPPE-II cutoffs increase with adjustment for gestational age. This phenomenon reflects the supplemental information provided by the gestational age groups.

SNAPs, mortality, and adjustment for gestational age

The observations that the lower the gestational age, the higher the risk of death and the higher the SNAP-II and SNAPPE-II prompted us to adjust for gestational age when evaluating the associations between the SNAPs and the risk of death. We did this in two ways for all SNAP-II and SNAPPE-II cut-offs. For all comparisons, the more extreme the cutoff, the stronger the prediction of death.

SNAP-II and SNAPPE-II decline with increasing gestational age more rapidly between weeks 23 and 26, than between weeks 26 and 27. Thus, these two illness severity scores carry with them information about gestational age and gestational age related phenomena. Since low gestational age, as well as each illness severity score, conveys information about mortality risk, adjusting for gestational age diminishes the SNAP contribution to mortality.

When the illness severity score is classified in relation to gestational age peers, such as whether or not it is in the highest quartile or decile for gestational age, adjusting for gestational age tended to increase the SNAP contribution to mortality. This suggests that gestational age was not a confounder here, but was probably an effect modifier ⁸.

Our comparing SNAP-IIs of infants to those of their peers within narrow gestational age strata, dichotomizing them based on this comparison, and then evaluating the total sample crudely approximates what would be seen if each child was assigned a Z score and then classified as above or below an arbitrary Z score. This approximation is limited by the use of an internal standard rather than the preferred external standard for a Z score. Despite limitations, though, our classifying infants as above or below the quartile or decile mark within each gestational age stratum provided valuable death-discriminating information.

Higher odds ratios with SNAPPE-II than with SNAP-II

Seven of the eight mortality odds ratios comparisons were higher for SNAPPE-II than for SNAP-II (Table 1). This is most likely a consequence of SNAPPE-II, but not SNAP-II, including information about intrauterine growth restriction, which is an independent predictor of mortality in preterm newborns^{9, 10}.

Predictive values

The predictive values positive (predicting death) were much smaller than the predictive values negative (predicting survival) (Table 1). This is typical of most predictors.

Inter-institutional differences

The higher the proportion of infants with a SNAP-II of 30 or more at an institution, the higher the mortality rate (Table 2). Some of the variation among NICUs represents phenomena demonstrated in Figure 1 (at all gestational ages, the higher the SNAP-II, the higher the risk of death).

We believe that some of the inter-institutional differences in mortality reflect different recruiting procedures. At some institutions, women admitted to the high-risk obstetrical service were enrolled before delivery, whereas at other institutions the child had to have a first ultrasound scan before the mother was asked to consent. Consequently, all of the very early deaths are included at prenatal-enrollment institutions, while none of the very early deaths are included at postnatal-enrollment institutions.

SNAP-II components

Although SNAP-II and SNAPPE-II include an item for repetitive seizures, in our sample of extremely low gestational age newborns, not one newborn had “multiple seizures confirmed or highly suspected.” No single component or group of components appeared to account for the institutional differences in the proportion of babies who had a SNAP-II of 30 or higher (Table 3). Thus, it is unlikely that medical care practices influenced SNAP-II or SNAPPE-II in this population of ELGANs.

Strengths and limitations

Samples defined by low birth weight tend to include intra-uterine growth restricted newborns who are gestationally older than others of the same or similar birth weights. When gestational age related phenomena are the focus, such as SNAP-II and SNAPPE-II, low birth weight samples can contribute to biased inferences¹¹. We have avoided these problems by enrolling newborns on the basis of gestational age and not birth weight.

Because of its large size, our study has the power to identify odds ratios of less than 2.0. Nevertheless, this was not an issue because all the odds ratios in Table 2 exceed this value.

We view the diversity of care characteristics among the 14 participating institutions to be an asset, and not a limitation. With 14 diverse institutions, our findings can be viewed as generalizable.

A recent study from the Neonatal Research Network has shown improved prediction of unfavorable outcome among preterm infants born at 22–25 weeks gestation when the gestational age variable is supplemented with information on the infant’s birthweight, sex, singleton status, and exposure to antenatal glucocorticoid¹². A simple calculator based on these data is available on the Internet (www.nichd.nih.gov/neonatalestimates). A formal comparison between this method and SNAP-II/SNAPPE-II is beyond the scope of this paper.

In summary, SNAP-II and SNAPPE-II predict death in our sample of infants born before the 28th week, even after adjusting for gestational age. Thus, we provide strong support for the claim that the death-discriminating information contained in SNAP-II and SNAPPE-II applies to the least mature.

Abbreviations

ELGAN	Extremely low gestational age newborn (<28wks)
NICU	Neonatal Intensive Care Unit
SNAP	Score for Neonatal Acute Physiology
SNAPPE	SNAP Perinatal Extension
VON	Vermont Oxford Network

Acknowledgments

Supported by a cooperative agreement with National Institute of Neurological Disorders and Stroke (NIH (1 U01 NS 40069-01A2) and a program project grant from the National Institute of Child Health and Human Development (NIH-P30-HD-18655). OD received funding from the European Union (LSHM-CT-2006-036534), the Wilhelm Hirte Stiftung (Hannover), and the Richard Saltonstall Charitable Foundation during the writing of this paper.

References

1. Richardson DK, Phibbs CS, Gray JE, McCormick MC, Workman-Daniels K, Goldmann DA. Birth weight and illness severity: independent predictors of neonatal mortality. *Pediatrics* 1993;91(5):969–975. [PubMed: 8474818]
2. Richardson DK, Corcoran JD, Escobar GJ, Lee SK. SNAP-II and SNAPPE-II: Simplified newborn illness severity and mortality risk scores. *J Pediatr* 2001;138(1):92–100. [PubMed: 11148519]
3. Zupancic JA, Richardson DK, Horbar JD, Carpenter JH, Lee SK, Escobar GJ. Revalidation of the Score for Neonatal Acute Physiology in the Vermont Oxford Network. *Pediatrics* 2007;119(1):e156–e163. [PubMed: 17158947]
4. Rautonen J, Makela A, Boyd H, Apajasalo M, Pohjavuori M. CRIB and SNAP: assessing the risk of death for preterm neonates. *Lancet* 1994;343(8908):1272–1273. [PubMed: 7910282]
5. Pollack MM, Koch MA, Bartel DA, Rapoport I, Dhanireddy R, El-Mohandes AA, et al. A comparison of neonatal mortality risk prediction models in very low birth weight infants. *Pediatrics* 2000;105(5):1051–1057. [PubMed: 10790462]
6. Gagliardi L, Cavazza A, Brunelli A, Battaglioli M, Merazzi D, Tandoi F, et al. Assessing mortality risk in very low birthweight infants: a comparison of CRIB, CRIB-II, and SNAPPE-II. *Arch Dis Child Fetal Neonatal Ed* 2004;89(5):F419–F422. [PubMed: 15321961]
7. Akobeng AK. Understanding diagnostic tests 1: sensitivity, specificity and predictive values. *Acta Paediatr* 2007;96(3):338–341. [PubMed: 17407452]
8. Leviton A, Blair E, Dammann O, Allred E. The wealth of information conveyed by gestational age. *J Pediatr* 2005;146(1):123–127. [PubMed: 15644836]
9. Eleftheriades M, Creatsas G, Nicolaides K. Fetal growth restriction and postnatal development. *Ann N Y Acad Sci* 2006;1092:319–330. [PubMed: 17308157]
10. Papageorgiou AT, Fratelli N, Leslie K, Bhide A, Thilaganathan B. Outcome of fetuses with antenatally diagnosed short femur. *Ultrasound Obstet Gynecol* 2008;31(5):507–511. [PubMed: 18286672]
11. Arnold CC, Kramer MS, Hobbs CA, McLean FH, Usher RH. Very low birth weight: a problematic cohort for epidemiologic studies of very small or immature neonates. *Am J Epidemiol* 1991;134(6):604–613. [PubMed: 1951265]

12. Tyson JE, Parikh NA, Langer J, Green C, Higgins RD. Intensive care for extreme prematurity--moving beyond gestational age. The New England journal of medicine 2008;358(16):1672–1681. [PubMed: 18420500]

Figure 1.

Box and whiskers plot of SNAPs at each week of gestational age presented separately for newborns who died in the first month and those who survived. The central tendency is indicated by the line close to the middle of the box, which is the median, and by the top and bottom of each box, which indicate the 25th and 75th centiles. The scatter of SNAP-IIs is indicated by the length of the vertical lines that emanate from the box, as well as by the dots, which identify outliers. The median line for the 27-week newborns who died is superimposed on the line for the 25th centile. * Wilcoxon rank-sum $p=0.003$; ** $p=0.001$; *** $p<0.001$; § $p=0.09$. The relationship between gestational age and SNAP-IIs was significantly different across gestational ages, with Chi-square p -values for trend of $p<0.0005$ for all observations, $p<0.0005$ for survivors, and $p=0.001$ for infants who died.

Table 1

The point estimate (and 95% confidence intervals) of the odds ratio of death during the first postnatal month associated with each of the 4 different measures of high SNAP-II and SNAPPE-II, as well as the predictive value positive and negative for each of these measures. The referent group for each set of analyses consists of all newborns whose SNAP-II or SNAPPE-II was lower.

Classification	Odds ratios (95% CIs)		Predictive values **	
	Unadjusted	Adjusted for GA *	Positive	Negative
SNAP-II				
Arbitrary cutoff (≥ 30)	5.9 (4.3, 8.1)	3.5 (2.5, 5.0)	29	93
Highest quartile for GA	2.4 (1.8, 3.3)	2.6 (1.9, 3.7)	21	90
Highest decile for GA	3.3 (2.3, 4.9)	4.0 (2.6, 6.2)	29	90
Z-score > 1	2.6 (1.7, 4.1)	3.0 (1.8, 4.7)	30	89
SNAPPE-II				
Arbitrary cutoff (≥ 45)	6.8 (4.9, 9.6)	3.9 (2.7, 5.7)	29	95
Highest quartile for GA	2.6 (1.9, 3.6)	3.0 (2.1, 4.2)	22	90
Highest decile for GA	3.3 (2.2, 4.8)	4.2 (2.7, 6.4)	29	90
Z-score > 1	3.3 (2.0, 5.2)	4.4 (2.6, 7.4)	36	89

* 23–24, 25–26 and 27 weeks

** not adjusted for gestational age

Table 2

The distribution of gestational ages and SNAP-II among newborns at each hospital of birth. The numbers in each of the cells are row percents. The hospitals are arranged in ascending order of the proportion of infants born at 23 and 24 weeks.

Hospital	Gestational age			SNAP-II		
	23–24	25–26	27	< 20	20–29	30+
A	7	48	45	55	34	10
B	12	40	49	77	12	12
C	21	53	26	34	28	38
D	23	38	40	49	26	26
E	23	54	23	40	26	34
F	24	44	33	40	37	24
G	27	44	29	62	22	16
H	27	49	24	51	24	25
I	29	44	28	55	19	25
J	30	46	23	31	25	44
K	30	37	33	54	24	22
L	32	51	17	52	17	31
M	35	42	23	48	16	36
N	39	39	22	49	27	23
Total	27	45	29	48	24	28

Table 3

The median value of each SNAP component at each hospital of birth.

Hospital	SNAP ≥ 30	Lowest BP	Lowest temp	Lowest serum pH	Total urine output	Worst P _a O ₂	Worst F _i O ₂	Lowest P _a O ₂ /F _i O ₂
J	44	23	95.7	7.2	9	49	35	1.51
C	38	23	96.0	7.2	16	53	40	1.38
M	36	25	97.3	7.3	8	55	42	1.33
E	34	25	97.2	7.3	14	52	51	1.06
L	31	22	96.4	7.3	10	64	40	1.62
D	26	25	96.5	7.3	24	50	40	1.35
H	25	24	97.1	7.2	14	49	50	1.26
I	25	23	97.3	7.3	14	58	42	1.45
F	24	24	96.4	7.3	16	58	55	1.21
N	23	26	95.8	7.3	10	53	35	1.60
K	22	23	97.0	7.3	17	59	50	1.39
G	16	23	97.2	7.3	20	53	31	1.72
B	12	26	97.2	7.3	22	58	30	1.81
A	10	24	96.7	7.3	18	59	39	2.01