Variability of Very Low Birth Weight Infant Outcome and Practice in Swiss and US Neonatal Units

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abstract

OBJECTIVES: Outcomes of very preterm infants vary considerably between health care facilities. Our objective was to compare outcome and practices between the Swiss Neonatal Network (SNN) and US members of the Vermont Oxford Network (US-VON).

METHODS: Retrospective observational study including all live-born infants with a birth weight between 501 and 1500 g as registered by SNN and US-VON between 2012 and 2014. We performed multivariable and propensity score-matched analyses of neonatal outcome by adjusting for case-mix, race, prenatal care, and unit-level factors, and compared indirectly standardized practices.

RESULTS: A total of 123 689 infants were born alive in 696 US-VON units and 2209 infants were born alive in 13 SNN units. Adjusted risk ratios (aRRs) for the composite "death or major morbidity" (aRR: 0.56, 95% confidence interval: 0.51–0.62) and all other outcomes were either comparable or lower in SNN except for mortality, for which aRR was higher (aRR: 1.28, 95% confidence interval: 1.09–1.50). Propensity score matching and restricting the analysis to infants for which we expect no survival bias, because both networks routinely initiate intensive care at birth, revealed comparable aRR. Variations in observed practices between SNN and US-VON were large.

CONCLUSIONS: The SNN units had a significantly lower risk ratio for death or major morbidity. Despite higher mortality, this difference is independent of survival bias. The higher delivery room mortality reflects the SNN practice to favor primary nonintervention for infants born <24 completed gestational weeks. We propose further research into which practice differences have the strongest beneficial impact.

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WHAT'S KNOWN ON THIS SUBJECT: The outcome variability among neonatal health care providers is substantial and has been shown to be associated with the variability of translating new evidence into practice. In neonatology, several perinatal practices have an established evidence base.

WHAT THIS STUDY ADDS: The risk for "death or major morbidity" is lower in Swiss neonatal units than in US Vermont Oxford Network units (0.56). This difference is robust and independent of survival bias. Swiss units follow established evidence closer for some perinatal practices.

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Comparing patient outcomes between hospitals, regions, or even nations carries the potential of finding possibilities for health care improvement. If 1 group shows better results at comparable or lower cost, a closer investigation is called for, particularly if the difference can be associated with a more reliable or more effective application of evidence-based practices. Such variations are likely to exist.[1] New evidence in medicine appears continuously and the variability of translating new evidence into practice is seen as one of the core reasons for the existing quality chasm between health care providers.[2]

In neonatology, the outcome variability between providers has a plethora of reasons. In various publications authors report differences in maternal baseline characteristics, case mix, hospital infrastructure, approach to initiation or redirection of intensive care in extremely preterm infants, social factors, race, and clinical care practices.[3–8] Only the lattermost constitute the target for quality improvement. To identify their potential, all other parts need to be eliminated, which is usually done in a cohort study setting. The cohorts need to be representative and their data well defined and complete, a target difficult to achieve. Usually randomized controlled trials (RCTs) are performed to avoid these difficulties by design. But if the intervention is complex, multicomponent, and dependent on local factors, assessment techniques involving the context may even be methodologically superior to RCTs.[9,10] In this study, we investigate such a complex context by using a cohort study setting to investigate differences in outcome and treatment practices based largely on RCTs.[11,12]

METHODS

Study Population

We included live-born children with a birth weight of 501 to 1500 g, born between 2012 and 2014 and registered by 1 of the 696 US members of the Vermont Oxford Network (US-VON) or by 1 of the 13 units of the Swiss Neonatal Network (SNN). Nine Swiss NICUs (encompassing 95% of the Swiss study population) transfer their data annually to the US-VON. Four step-down units collected data simultaneously but were added separately to this study. Delivery room (DR) deaths and admissions to a unit within 28 days of age were included. Data were collected electronically from birth until death or first discharge home from the hospital by all participating units by using the same data definition, plausibility, and completeness checks and subsequent repeated challenge until corrected. All items were defined in a publicly available manual.[13]

Data collection and evaluation for this study were approved by the Swiss ethical review boards (KEK-ZH-Nr2014-0552) and the Committee on Human Research at the University of Vermont. No protected health care information was collected.

Outcomes

Outcomes were strictly defined and potentially adaptable by changes of process or unit level structure (ie, relevant for quality improvement).[14,15] The selected outcomes have been tested for their ability to assess neonatal quality of care.[16] The following proportions of newborns with the respective outcome (ie, cumulative incidence proportion over a 3-year time span) were based on infants admitted to a neonatal unit: in-hospital mortality (all deaths without DR deaths); late onset sepsis with clear clinical evidence of infection as well as at least 1 microbiologically relevant positive result from blood cultures (including coagulase negative staphylococci and fungal pathogens) obtained after day 3 of age, with day of birth as day 1, regardless of the time of birth; necrotizing enterocolitis (NEC), severe intraventricular hemorrhage (sIVH), severe retinopathy of prematurity (sROP), and chronic lung disease (CLD) were defined as previously published.[17] The composite outcomes "death or major morbidities" combined all deaths and all morbidities listed above, "any mortality" combined all deaths, and "any major morbidity" combined all morbidities listed above.

Confounders

We adjusted outcome comparisons for confounding. The full set of confounders, including a combination of patient-level case-mix parameters, race, prenatal care, and 6 unit-level factors, was defined a priori but added incrementally to display their individual effect. Case-mix parameters consisted of variables that were known to be associated with the outcomes and thus may introduce confounding. The covariates also had to be outside of the influence of the NICUs (ie, not bearing a potential for quality improvement) and are as follows: gestational age (GA), gestational age squared (GA^2), small for gestational age (SGA), male sex, multiple birth, major malformation, chorioamnionitis, and maternal hypertension. GA was calculated based on ultrasound examinations during the first trimester of pregnancy and defined as postmenstrual age in weeks and days. GA^2 was added to provide a better model for the nonlinear dependency of most neonatal outcomes on GA. SGA was defined as previously published.[17] Major congenital malformation was defined as being the primary cause of death or requiring surgery.

Chorioamnionitis was recorded when diagnosed clinically or histologically, maternal hypertension when chronic or pregnancy-induced, with or without edema and proteinuria. Race was based on the mother's origin. Prenatal care included "any obstetrical prenatal care." The following 6 unit-level factors were chosen for their noteworthy difference between the US-VON and the SNN: hospital ownership (government, nonprofit, investor, other), NICU type (type A, B, or C), availability of single rooms, pediatric resident, or neonatal fellow, and unit size. NICU type A have a restriction on assisted ventilation or perform minor surgery only. Type B are without restriction on assisted ventilation and perform major surgery. Type C additionally perform cardiac surgery requiring bypass for newborn infants. Outborn, defined as previously published,[7] was not used to exclude infants or as risk adjustment as it is known to bear potential for improvement.

Practices

Any antenatal steroids and any form of vaginal delivery were recorded. Respiratory practices in the NICU required at least 1 period of 12 hours. Postnatal systemic corticosteroids were to treat or prevent CLD. Human milk feeding refers to infants that were fed with human milk alone or in combination with either fortifier or formula.

Data Completeness

The cohorts represented 84% of all US live births and 95% of all Swiss life births, respectively, as determined by comparison with the birth registry of the Centers for Disease Control and Prevention national vital statistics report for the United States and the Swiss Federal Statistical Office. Unit-level data were mandatory and available for all units. Outcome data were missing for sROP (16.7%), sIVH (8.6%), late onset sepsis (3.5%), and CLD (2.7%). Infants missing data for sROP were considered as having no sROP if they were ≥32 weeks' GA at birth in the composites "death or major morbidities" and "any major morbidity," resulting in 8.4% missing data. All other data were complete or missing <1%. Outcomes were analyzed excluding the infants missing the respective item.

TABLE 1 Baseline Patient Characteristics

Patient Characteristics	US-VON	SNN
Infants 501–1500 g birth wt	123 689	2209
Mean GA (SD)	28.6 (2.9)	29.2 (2.9)
Mean birth wt (SD)	1058 (285.9)	1087 (284.2)
SGA	21.4%	27.7%
Male sex	50.7%	50.7%
Multiple birth (eg, twins, triplets)	26.9%	34.3%
Major malformations	5.0%	4.4%
Chorioamnionitis	12.7%	25.9%
Maternal hypertension	31.2%	23.0%
Prenatal care	96.2%	100%
Inborn	86.0%	94.9%
Apgar1 <4	28.6%	27.5%
Apgar5 <4	8.6%	9.8%
Ethnicity, Asian	4.4%	3.2%
Ethnicity, Black	29.9%	3.7%
Ethnicity, white	55.0%	92.9%
Ethnicity, other	10.5%	0.2%
Total length of stay in d (SD)[a]	71.1 (42.4)	65.0 (40.5)

[a] Mean value of infants discharged from the hospital alive.

Statistical Methods

A multivariable logistic regression was used to estimate adjusted odds ratios that were converted to risk ratios (RRs) by using the method from Zhang and Yu.[18] We performed propensity score matching to see if network size or confounding had an impact on the results. Propensity scores (ie, the probability of being in the SNN cohort) were estimated from a logistic regression model that included the covariates GA, GA^2, SGA, sex, multiple birth, race, and hospital ownership. Observations from the SNN cohort were matched to an entry from the US-VON having the closest propensity score (Supplemental Table 5). Practices were adjusted for case mix and indirectly standardized with US-VON infants as reference population. Analysis was repeated among a restricted cohort of infants between 25 + 0 and 29 + 6 weeks' GA. All statistical analyses were performed by using R Version 3.4.[19]

RESULTS

A total of 123 689 very low birth weight (VLBW) infants born alive in 696 US-VON units between 2012 and 2014 were compared with 2209 VLBW infants born alive in 13 SNN units during the same period. Baseline patient characteristics (Table 1) differ in several aspects. SNN mean GA limited by birth weight was 0.6 weeks higher and there were 6% more infants SGA than in US-VON units. VLBW infants from Switzerland are generally smaller than those from other origins.[20] The SNN had a higher proportion of multiple births (34.3% vs 26.9%) and twice the amount of diagnosed chorioamnionitis (25.9% vs 12.7%); however, SNN had fewer cases of maternal hypertension (23% vs 31.2%), more inborn infants (94.9% vs 86.0%), and a different racial composition.

On a unit level, the SNN units had fewer admissions per year, were mostly owned by the government, had a comparable degree of specialization, a lower proportion of infants cared for in single rooms,

TABLE 2 Baseline Unit Characteristics

Unit Characteristics	US-VON, No. (%)	SNN, No. (%)
N (units/infants 501–1500 g birth wt)	696	13
Mean total admissions per y (SD)	514 (328)	440 (212)
Cranial ultrasound available	695 (100)	13 (100)
Echocardiography available	693 (99.7)	13 (100)
PDA ligation available	350 (50.4)	8 (61.5)
ROP screening available	685 (98.7)	13 (100)
Nasal CPAP available	693 (99.7)	13 (100)
Assisted ventilation available	694 (99.9)	10 (76.9)
Hospital owner		
Government	57 (8.2)	12 (92.3)
Nonprofit	520 (74.8)	1 (7.7)
Investor	102 (14.7)	0 (0)
Other	16 (2.3)	0 (0)
NICU type		
A	291 (41.8)	4 (30.8)
B	297 (42.7)	5 (38.5)
C	108 (15.5)	4 (30.8)
Level obstetric service		
Level I	6 (0.9)	0 (0)
Level II	177 (25.8)	3 (23.1)
Level III	503 (73.3)	10 (76.9)
Percent cared for in single rooms, %		
<10	437 (63)	12 (92.3)
10–50	49 (7.1)	1 (7.7)
50–90	35 (5)	0 (0)
≥90	173 (24.9)	0 (0)
Surgery on site	389 (56)	9 (69.2)
Pediatric resident in NICU	227 (32.7)	13 (100)
Neonatology fellow in NICU	144 (20.7)	12 (92.3)
Other residents in NICU	253 (36.4)	7 (53.8)

CPAP, continuous positive airway pressure; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity.

and higher proportions of pediatric residents and neonatal fellows (Table 2).

The crude proportion of the composite primary outcome "death or major morbidity" was lower in SNN than in US-VON (33.7% vs 46.9%, Table 3). Incremental adjustment for patient and unit-level factors known for their capacity to influence local outcome revealed a significantly lower final adjusted risk ratio (aRR) for death or major morbidity in SNN (0.56, 95% confidence interval [CI]: 0.51–0.62). We performed propensity score matching to test if the 56-fold higher number of infants registered in US units and the major differences between SNN and US-VON presented in Table 1 had an influence on outcome not captured by adjustment.[21] Propensity score matching resulted in 1591 SNN and US-VON cases, matched 1:1 (Supplemental Table 5), and an aRR of 0.69 (CI: 0.63–0.75).

Crude DR mortality was higher in SNN (5.2%) versus US-VON (2.3%), whereas in-hospital mortality was lower in SNN (7.5% vs 9.0%), resulting in an overall higher mortality for SNN (12.3% vs 11.0%, Table 4). All other components of the composite outcome (ie, NEC, late onset sepsis, sIVH, CLD, and sROP) had lower proportions in SNN versus US-VON. When stratified into GA groups, DR mortality was higher among SNN infants up to 28 + 6 weeks' GA. SNN also had a higher proportion of late onset sepsis at 25 + 0 weeks' GA to 26 + 6 weeks' GA and >31 + 6 weeks' GA. All other morbidities were either comparable or lower in SNN compared with US-VON.

The aRR for DR mortality was significantly higher for SNN infants. The RR for in-hospital mortality was comparable, whereas all RRs for morbidities (as composite and individual factors) were significantly lower in SNN (Table 4). In comparison with the crude RRs, the adjustments for patient level factors (case mix and race) increased the RR for mortality and morbidities

TABLE 3 Outcome Variation as Crude Proportions of US-VON and SNN

Outcome	Unit	Proportions of All Infants, %	RR (95% CI)			
			Crude	With Patient-Level Adjustment	With Prenatal Care Adjustment	With Unit Level Adjustment (Final OR)
Death or major morbidity	US-VON	46.9	0.72 (0.68–0.77)	0.7 (0.64–0.76)	0.7 (0.64–0.76)	0.56 (0.52–0.63)
	SNN	33.7				
Any mortality	US-VON	11.0	1.12 (1–1.25)	1.3 (1.12–1.51)	1.31 (1.13–1.52)	1.28 (1.09–1.50)
	SNN	12.3				
Any major morbidity (survivors only)	US-VON	39.1	0.58 (0.53–0.64)	0.63 (0.56–0.7)	0.63 (0.56–0.7)	0.49 (0.44–0.55)
	SNN	22.8				

Adjusted ORs of outcome in SNN versus US-VON starting with crude (unadjusted) data and incrementally adding patient level adjustment, prenatal care, and unit level adjustment (final OR). OR, odds ratio.

TABLE 4 Unadjusted and Adjusted Outcome Variability Between SNN and US-VON Stratified by GA Groups and in Total (All Infants)

Outcome	Unit	Proportions						Final aRR (95% CI)	Restricted aRR 25–29 wk GA (95% CI)
		GA, wk					In Total (All Infants)		
		<25	25–26	27–28	29–31	>31			
No. infants	US-VON	15 181	22 017	29 329	40 827	16 335	123 689	—	—
	SNN	185	349	453	821	401	2209		
Death or major morbidity[a]	US-VON	93.1%	71.7%	43.6%	24.1%	17.8%	46.9%	0.56 (0.52–0.63)	0.57 (0.51–0.64)
	SNN	90.8%	63.8%	32.7%	15.5%	9.0%	33.7%		
Any mortality[a]	US-VON	43.3%	14.6%	6.1%	3.4%	4.6%	11.0%	1.28 (1.09–1.50)	1.07 (0.85–1.35)
	SNN	68.5%	21.5%	7.5%	3.3%	2.5%	12.3%		
DR mortality[a]	US-VON	13.0%	1.0%	0.6%	0.6%	1.2%	2.3%	3.36 (2.42–4.45)	1.75 (0.90–3.41)
	SNN	49.7%	2.9%	1.5%	0.6%	0.2%	5.2%		
In-hospital mortality[b]	US-VON	34.7%	13.7%	5.5%	2.8%	3.4%	9.0%	1.10 (0.91–1.33)	1.03 (0.80–1.31)
	SNN	37.0%	19.2%	6.1%	2.7%	2.2%	7.5%		
Any major morbidity[c]	US-VON	87.5%	66.5%	39.5%	20.8%	12.2%	39.1%	0.49 (0.44–0.55)	0.51 (0.45–0.58)
	SNN	70.7%	53.3%	26.8%	12.0%	6.0%	22.8%		
NEC[c]	US-VON	9.3%	6.5%	4.4%	2.4%	1.3%	4.0%	0.33 (0.21–0.50)	0.28 (0.16–0.48)
	SNN	10.3%	1.8%	2.4%	0.9%	0.5%	1.5%		
Late-onset sepsis[c]	US-VON	30.1%	17.4%	8.7%	3.5%	1.5%	9.0%	0.81 (0.67–0.98)	0.80 (0.64–0.99)
	SNN	29.3%	20.8%	8.4%	2.8%	1.8%	7.1%		
sIVH[c]	US-VON	20.8%	11.1%	4.8%	1.8%	0.8%	5.7%	0.75 (0.58–0.98)	0.77 (0.57–1.04)
	SNN	6.9%	8.8%	4.8%	1.9%	1.0%	3.5%		
CLD[c]	US-VON	70.2%	51.1%	27.4%	11.7%	6.5%	25.9%	0.41 (0.35–0.47)	0.40 (0.34–0.48)
	SNN	49.1%	29.5%	15.0%	5.7%	2.0%	11.8%		
sROP[c]	US-VON	31.8%	12.4%	2.4%	0.6%	0.3%	6.1%	0.25 (0.16–0.38)	0.22 (0.12–0.38)
	SNN	13.8%	5.2%	0.0%	0.0%	0.0%	1.4%		

sIVH is considered as intra- or periventricular hemorrhage grade 3–4, and sROP is considered as retinopathy of prematurity stages 3–4. —, not applicable.

[a] All infants.

[b] Infants admitted.

[c] Infants discharged from the hospital alive.

attributing a lower risk to SNN infants, whereas the adjustment for unit level factors (hospital ownership, NICU type, physician staffing, and unit size) decreased the RRs. The adjustment for prenatal care had no effect on the RRs (Table 3).

The difference in DR death between SNN and US-VON units is highest for infants born <25 + 0 weeks' GA (49.7% vs 13.0%, Table 4). The infants who died in the DR did not survive to develop sIVH, NEC, late onset sepsis, CLD, and sROP, forming a survival bias toward the SNN for these morbidity outcomes. However, a logistic regression using a restricted cohort of infants born between 25 + 0 and 29 + 6 weeks' GA (N = 75 383), for which both SNN and US-VON generally initiate intensive care, resulted in almost the same aRR for all outcomes as for the whole cohort except overall mortality, which was no longer significantly different (Table 4).

Indirect standardization revealed higher than expected use of antenatal steroids, of less invasive DR interventions, of less invasive respiratory practices, and of maternal milk feeding at discharge in Swiss units (Fig 1). Lower ratios were observed for vaginal delivery, surfactant use at any time, oxygen requirement after DR, and for postnatal steroid application to treat or prevent CLD. Again, restriction to infants between 25 + 0 weeks' GA and 29 + 6 weeks' GA had an almost identical result (Supplemental Fig 2).

DISCUSSION

In this study, we compare practice and outcome between 2 neonatal networks from the United States and Switzerland representing 84% and 95% of the population, respectively. Both networks apply the same definitions for prospective data collection and combine patient and unit-level data, which allowed adjusting outcomes for patient and unit-level parameters. The aRR for "death or major morbidity," for "any major morbidity," as well as for all individual morbidities favored SNN, whereas those for mortality favored US-VON. Propensity score matching for the most effective confounders confirmed the result and cohort restriction to 25 to 29 weeks' GA (in which intensive care is initiated for all infants) removed the significant difference in mortality but confirmed the difference in morbidities (Table 4). We were thus able to demonstrate that the differences in outcome between SNN and US-VON units are robust and largely unaffected by survival bias or competing risk.

For infants who are born <28 + 0 weeks' GA, crude DR and in-hospital mortality are higher in the SNN. The largest difference lies in DR mortality for infants born <25 + 0 weeks' GA (49.7% vs 13.0% in US-VON units). Swiss guidelines published in 2011 recommend a priori comfort care

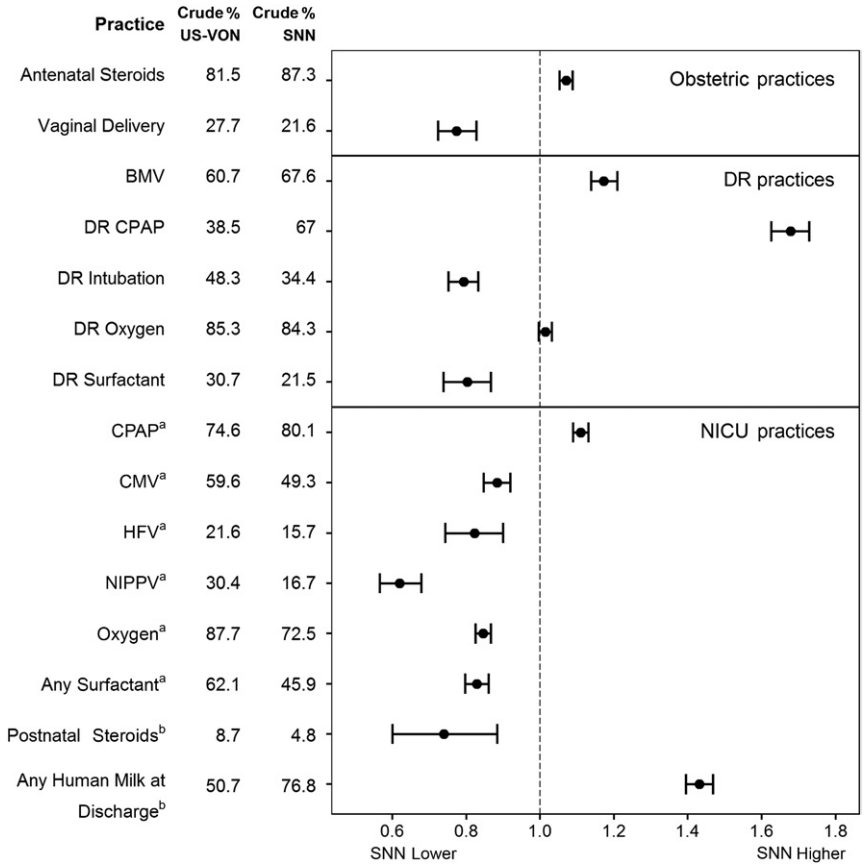

FIGURE 1

Obstetrical, DR, NICU, and nutritional practices as crude cumulative incidence proportions of both SNN and US-VON and indirectly standardized, case mix- adjusted observed to expected ratios. The reference collective is as follows: [a] proportion of infants admitted, [b] proportion of infants discharged from the hospital alive. BMV, bag or mask ventilation; CMV, conventional mechanical ventilation; HFV, high frequency ventilation; NIPPV, nasal intermediate positive pressure ventilation.

for live births at 22 weeks' GA, comfort care with the possibility of intensive care in the presence of positive prognostic factors at 23 weeks' GA, and intensive care with the possibility of comfort care in the presence of negative prognostic factors at 24 weeks' GA, respectively.[22] An analysis of all neonatal deaths in Switzerland during the period of 2012–2015 revealed that decision-making regarding initiation of treatment was based almost exclusively on GA, mirroring the results of the EPIPAGE-2 study.[23,24] The DR mortality for infants born <25 + 0 weeks' GA thus reflects the Swiss practice of applying a priori comfort care for almost all infants born <24 + 0 weeks' GA.[24] After admission to NICU, 94% of deaths at <28 weeks' GA occurred after redirection of care after end-of-life decision-making. Different approaches to decision-making in Switzerland and the United States may have contributed to the higher in-hospital mortality of infants born <28 weeks' GA in Swiss units. Such differences are known to exist even between different Swiss regions[25] and may reflect, among other, the effect of the linguistic region (German, French, or Italian) on the attitudes toward extreme prematurity.[26]

US-VON has a long history of collecting data that are associated with outcome.[11] We were thus able to adjust for known important perinatal confounders often used in literature[3,4,7,15,27] and not bearing a potential for quality improvement. Any additional confounding will therefore likely have taken place during pregnancy and requires a difference in prevalence between the 2 networks. We therefore listed the most important known such parameters in Supplemental Table 6. Whereas infant mortality, health care expenditure per capita, and proportion of VLBW infants of all births are higher in the United States, both nations are highly developed, and have similar overall life expectancy and per capita gross domestic product rank. Contrary to Switzerland being perceived as a homogenous high-income community, socioeconomic diversity is present. For instance, 36% of the Swiss population have an immigrant background.[28] We would therefore not expect main differences between the 2 nations to originate in the proportion of wealthy patients, but in overall size, racial differences, and having a mandatory health insurance. In this study, the effect of population size was analyzed by using propensity score matching, and race was adjusted for, however, not excluding possible effects from finer distinctions (eg, ethnic or genetic variation). Adjusting for prenatal care had no effect on the analyzed outcomes but constitutes only a crude measure of attendance because there is no consensus about what constitutes good or optimal maternity care.[29]

The proportion of the self-reported US population who are obese is almost 3 times as high as in Switzerland. Two recent retrospective studies, with >180 000 pregnancies each, have however found no adverse association between BMI and GA at delivery for preterm birth.[30,31] BMI-associated type 2 diabetes, however, is associated with adverse outcome of preterm birth.[32] Further differences for which we have no data available to measure an effect are smoking and

alcohol consumption, both of which are higher in Switzerland. These factors are likely to have a general influence on newborn outcome. But apart from a possible influence of type 2 diabetes, they do not explain why RRs should favor the SNN.

We observed a wide variability in some of the obstetric, DR, NICU, and nutritional practices between the SNN and US-VON. After adjustment for case mix and indirect standardization using US-VON infants as reference, the SNN had a higher than expected use of antenatal steroids, a practice well-known to improve outcome.[33] In the DR, stabilization on continuous positive airway pressure rather than intubation was higher in the SNN, for which recent large trials reveal a lower risk of CLD or death.[34] On the ward, the SNN also used less aggressive ventilation techniques but there is no comparable evidence to support a beneficial impact, although the use of these techniques also has grown in US-VON.[7] The same was observable for vaginal delivery, which was less often performed in the SNN without known evidence but paralleled by a decrease of use in the US-VON. The SNN also used less systemic postnatal steroids, which carry an increased risk of adverse short-term and neurodevelopmental outcomes.[35] The higher ratio of partial human milk feeding at discharge in SNN will have had no immediate impact on the outcome at discharge of primary hospitalization but may indicate a higher breastfeeding proportion during hospital stay, which is known to be beneficial.[36,37]

The strength of this study lies in the size of the population, the high cohort representation, the homogeneity of the data collection, and the combination of patient and unit-level data. Limitations are given by the type of study; a cohort study can never rule out all confounding and the ability of risk adjustment to isolate relevant outcome differences is limited.[27] The presented results hence do not intend to infer causality on the part of practice difference but reveal a potential for possible change benefiting the patients to be further investigated. We addressed the limitations by adding propensity score matching and by listing the most likely factors alternatively associated with the differences in outcome. Further limitations are incomplete cohort representation, lack of discrimination in the variables for prenatal care and race, reporting only short-term outcome, and the partially missing outcome data, particularly for sROP and sIVH.

CONCLUSIONS

ARRs for the composite outcome "death or major morbidity" as well as for several neonatal morbidities favored the SNN. DR mortality was higher in SNN, largely because most infants in SNN <24 + 0 weeks' GA received a priori comfort care, which does not coincide with the current Swiss guidelines. Propensity score matching as well as cohort restriction confirmed the result of the primary outcome and its independence of survival bias. The SNN units appear to follow established evidence closer for some of the observed practices, whereas other practices are missing a clear evidence base. We propose further research into which practice differences have the strongest beneficial impact.

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ABBREVIATIONS

aRR: adjusted risk ratio
CI: confidence interval
CLD: chronic lung disease
DR: delivery room
GA: gestational age
GA^2: gestational age squared
NEC: necrotizing enterocolitis
RCT: randomized controlled trial
RR: risk ratio
SGA: small for gestational age
sIVH: severe intraventricular hemorrhage
SNN: Swiss Neonatal Network
sROP: severe retinopathy of prematurity
VLBW: very low birth weight
US-VON: US members of the Vermont Oxford Network

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