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Increased frequency of retinopathy of prematurity over the last decade and significant regional differences

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ABSTRACT.

Purpose: **Retinopathy of prematurity (ROP) causes childhood blindness globally in prematurely born infants. Although increased levels of oxygen supply lead to increased survival and reduced frequency of cerebral palsy, increased incidence of ROP is reported.**

Methods: **With the help of a Swedish register for ROP, SWEDROP, national and regional incidences of ROP and frequencies of treatment were evaluated from 2008 to 2015 (n = 5734), as well as before and after targets of provided oxygen changed from 85–89% to 91–95% in 2014.**

Results: **Retinopathy of prematurity (ROP) was found in 31.9% (1829/5734) of all infants with a gestational age (GA) of <31 weeks at birth and 5.7% of the infants (329/5734) had been treated for ROP. Analyses of the national data revealed an increased incidence of ROP during the 8-year study period ($p = 0.003$), but there was no significant increase in the frequency of treatment. There were significant differences between the seven health regions of Sweden, regarding both incidence of ROP and frequency of treatment ($p < 0.001$). Comparison of regional data before and after the new oxygen targets revealed a significant increase in treated ROP in one region [OR: 2.24 (CI: 1.11–4.49), $p = 0.024$] and a borderline increase in one other [OR: 3.08 (CI: 0.99–9.60), $p = 0.052$].**

Conclusion: **The Swedish national ROP register revealed an increased incidence of ROP during an 8-year period and significant regional differences regarding the incidence of ROP and frequency of treatment.**

Key words: incidence – oxygen – retinopathy of prematurity – treatment

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Introduction

Retinopathy of prematurity (ROP) is a potentially preventable cause of childhood blindness, and its incidence globally is increasing – mainly in middle-income countries (Blencowe et al. 2016). Low GA at birth is a major risk factor on which most screening programmes are based. However, insufficient quality of neonatal care and especially control of oxygen supply are essential risk factors and in settings with poor care, screening of more mature infants is required to identify those who need treatment. Incidence of ROP and frequency of treatment for ROP in Sweden have been monitored over many years with the help of population-based studies and a national registry, SWEDROP (Holmström et al. 1993, 2012, 2015, 2016; Larsson & Holmström 2002; Austeng et al. 2009). Based on these, inclusion criteria in the Swedish screening programme have been repeatedly adjusted, and since 2012 infants with GA <31 weeks are screened (Holmström et al. 1993, 2016; Larsson & Holmström 2002).

The optimal level of oxygen supply to preterm infants is still unknown. Excessive oxygen supplementation was early identified as a risk factor for ROP and restricted oxygen delivery reduced ROP but increased the rates of mortality (Avery 1960) and cerebral palsy (McDonald 1964). Recently, a meta-analysis - the Neonatal Oxygen Prospective Meta-Analysis (NeOProM) (Saugstad & Aune 2014) – of five randomized controlled trials similarly designed, was performed, comparing

the results of lower (85–89%) and higher (91–95%) pulse oxygen saturation (SpO_2) targets. With SpO2 targets below 90% fewer infants needed ROP treatment but mortality was increased (BOOST II United Kingdom, Australia, New Zealand Collaborative Groups 2013; BOOST-II Australia and United Kingdom Collaborative Group 2016). Based on these results, the SpO2 target range was gradually increased to 91–95% during 2014 and, with a few exceptions, implemented in Sweden in 2015.

The aim of this study was, using the Swedish ROP register data, to evaluate national and regional ROP frequency and treatment in Sweden over the last decade, as well as before and after the change in SpO2 target levels in 2014.

Materials and Methods

Sweden has seven geographical healthcare regions, each with one university/regional hospital. Screening for ROP was undertaken in all hospitals with neonatal intensive care units, and treatment was performed at each of the seven university hospitals. Classification of ROP followed international recommendations (International Committee for the Classification of Retinopathy of Prematurity 2005) and the criteria for treatment followed the recommendations of the Early treatment of Retinopathy of Prematurity (ETROP) study (Early Treatment for Retinopathy of Prematurity Cooperative Group 2003). Mild ROP was defined as stages 1–2, and severe ROP as stages 3–5.

Guidelines for screening for ROP in Sweden were changed in July 2012 from including infants with a GA of <32 weeks to including only infants with a GA of <31 weeks at birth (Holmström et al. 2012). For comparison of incidence of ROP and frequency of treatment over the years, only infants born with GA <31 weeks were included in the final study population. For calculation of national coverage of SWEDROP, comparison with the Swedish neonatal quality register (SNQ) was performed.

Each infant was classified according to region. Infants who had been moved between different hospitals were classified as belonging to the region where they had spent the majority of their time before a postmenstrual age (PMA) of 31 weeks, corresponding to the PMA

Table 1. Background data of the total study population of 5734 infants with a gestational age (GA) of <31 weeks, during the study period 2008–2015.

	2008 n = 698	2009 n = 695	2010 n = 657	2011 n = 705	2012 n = 729	2013 n = 717	2014 n = 763	2015 n = 770	Total n = 5734
GA, w, mean (range)	27.8 (22–30)	27.6 (22–30)	27.6 (22–30)	27.6 (22–30)	27.7 (22–30)	27.5 (22–30)	27.6 (22–30)	27.5 (21–30)	27.6 (21–30)
GA									
21	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.0)
22	7 (1.0)	4 (0.6)	3 (0.5)	8 (1.1)	8 (1.1)	8 (1.1)	9 (1.2)	10 (1.3)	57 (1.0)
23	21 (3.0)	24 (3.5)	20 (3.0)	18 (2.6)	24 (3.3)	30 (4.2)	32 (4.2)	33 (4.3)	202 (3.5)
24	27 (3.9)	46 (6.6)	37 (5.6)	53 (7.5)	30 (4.1)	31 (4.3)	40 (5.2)	59 (7.7)	323 (5.6)
25	52 (7.4)	63 (9.1)	55 (8.4)	47 (6.7)	67 (9.2)	55 (7.7)	66 (8.7)	68 (8.8)	473 (8.2)
26	66 (9.5)	79 (11.4)	91 (13.9)	57 (8.1)	75 (10.3)	104 (14.5)	73 (9.6)	82 (10.6)	627 (10.9)
27	103 (14.8)	91 (13.1)	72 (11.0)	104 (14.8)	91 (12.5)	95 (13.2)	112 (14.7)	69 (9.0)	737 (12.9)
28	118 (16.9)	93 (13.4)	104 (15.8)	125 (17.7)	111 (15.2)	114 (15.9)	116 (15.2)	127 (16.5)	908 (15.8)
29	127 (18.2)	135 (19.4)	137 (20.9)	137 (19.4)	130 (17.8)	138 (19.2)	142 (18.6)	149 (19.4)	1095 (19.1)
30	177 (25.4)	160 (23.0)	138 (21.0)	156 (22.1)	193 (26.5)	142 (19.8)	173 (22.7)	172 (22.3)	1311 (22.9)
Birthweight, g, mean (range)	1139 (307–2356)	1125 (400–2220)	1109 (420–1947)	1121 (382–2090)	1146 (340–2842)	1090 (415–1975)	1113 (387–2364)	1089 (420–2445)	1116 (307–2842)
Female gender, n (%)	306 (43.8)	301 (43.3)	318 (48.4)	339 (48.1)	347 (47.6)	338 (47.1)	324 (42.5)	329 (42.7)	2602 (45.4)
ROP, n (%)	187 (26.8)	242 (34.8)	204 (31.1)	210 (29.8)	217 (29.8)	233 (32.5)	253 (33.2)	283 (36.8)	1829 (31.9)
ROP level									
0	511 (73.2)	453 (65.2)	453 (68.9)	495 (70.2)	512 (70.2)	484 (67.5)	510 (66.8)	487 (63.2)	3905 (68.1)
1	49 (7.0)	65 (9.4)	52 (7.9)	67 (9.5)	81 (11.1)	75 (10.5)	66 (8.7)	89 (11.6)	544 (9.5)
2	71 (10.2)	92 (13.2)	59 (9.0)	80 (11.3)	84 (11.5)	85 (11.9)	100 (13.1)	95 (12.3)	666 (11.6)
3	66 (9.5)	80 (11.5)	90 (13.7)	62 (8.8)	51 (7.0)	70 (9.8)	85 (11.1)	93 (12.1)	597 (10.4)
4	0 (0.0)	4 (0.6)	2 (0.3)	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	3 (0.4)	11 (0.2)
5	1 (0.1)	1 (0.1)	1 (0.2)	0 (0.0)	1 (0.1)	2 (0.3)	2 (0.3)	3 (0.4)	11 (0.2)
Treated ROP, n (%)	36 (5.2)	43 (6.2)	45 (6.8)	31 (4.4)	30 (4.1)	40 (5.6)	45 (5.9)	59 (7.7)	329 (5.7)

ROP = retinopathy of prematurity.

when the first signs of ROP may be detected (Holmström et al. 2012).

The data on various aspects of screening and treatment for ROP were extracted from SWEDROP – a national web-based ROP register (Holmström et al. 2012).

The study was performed according to the Declaration of Helsinki with approval by the ethics committee of the Faculty of Medicine, Uppsala University, Sweden.

Statistical analysis

The study population is presented descriptively, using mean and range for numerical variables and absolute and relative frequencies for categorical variables. The tables are stratified by year (Table 1) and by region (Table 2). To analyse the change in GA and birthweight (BW) over the study period, linear regression models were used with year as a numeric variable. The changes in incidence of ROP, severe ROP and treated ROP over the study period were analysed using logistic regression models – one with year as the only independent factor, and one with adjustment for GA and BW. The same models were also applied within each of the seven regions. In addition, the same models were used to analyse the difference between the seven regions with respect to GA, BW (linear regression), ROP, severe ROP and treated ROP (logistic regression adjusted for GA and BW). During 2014, new routines regarding oxygen administration aiming to increase the level to 91–95% from previously 88–92% were implemented in most parts of Sweden. Therefore, an analysis was performed comparing the proportion of infants treated for ROP in 2015 (after the implementation) with the years before the change of oxygen routines (2008–2013), using a logistic regression model with the dummy variable pre–post, with GA and BW as independent variables. The analysis was performed for the total population, as well as for each region. The results are illustrated using Shewart-charts where the boundaries for *no change* are defined as mean ± 2 * standard deviation of the prechange yearly proportions. All reported results are the point estimates (odds ratio or mean) with 95% confidence intervals and nominal p-values. No adjustment

Table 2. Background data of the total study population of 5734 infants, divided by region, during the study period 2008–2015.

	Region 1 (n = 511)	Region 2 (n = 1424)	Region 3 (n = 1053)	Region 4 (n = 968)	Region 5 (n = 510)	Region 6 (n = 1008)	Region 7 (n = 158)	Unknown (n = 102)	Total (n = 5734)
GA, w, mean (range)	27.5 (22–30)	27.7 (22–30)	27.5 (22–30)	27.6 (22–30)	27.6 (23–30)	27.5 (21–30)	27.7 (22–30)	27.3 (22–30)	27.6 (21–30)
Birthweight, g, mean (range)	1083 (307–2364)	1128 (458–2240)	1112 (410–2840)	1129 (382–2280)	1109 (385–2090)	1122 (340–2842)	1108 (500–1990)	1038 (460–1665)	1116 (307–2842)
Female gender, n (%)	242 (47.4)	644 (45.2)	511 (48.5)	411 (42.5)	224 (43.9)	465 (46.1)	66 (41.8)	39 (38.2)	2602 (45.4)
Year									
2008	62 (12.1)	157 (11.0)	139 (13.2)	114 (11.8)	77 (15.1)	117 (11.6)	24 (15.2)	8 (7.8)	698 (12.2)
2009	63 (12.3)	191 (13.4)	120 (11.4)	104 (10.7)	54 (10.6)	115 (11.4)	20 (12.7)	28 (27.5)	695 (12.1)
2010	74 (14.5)	171 (12.0)	101 (9.6)	73 (7.5)	67 (13.1)	137 (13.6)	8 (5.1)	26 (25.5)	657 (11.5)
2011	57 (11.2)	173 (12.1)	122 (11.6)	126 (13.0)	60 (11.8)	141 (14.0)	20 (12.7)	6 (5.9)	705 (12.3)
2012	54 (10.6)	191 (13.4)	123 (11.7)	133 (13.7)	75 (14.7)	120 (11.9)	24 (15.2)	9 (8.8)	729 (12.7)
2013	58 (11.4)	167 (11.7)	156 (14.8)	131 (13.5)	53 (10.4)	127 (12.6)	19 (12.0)	6 (5.9)	717 (12.5)
2014	75 (14.7)	184 (12.9)	146 (13.9)	137 (14.2)	62 (12.2)	128 (12.7)	19 (12.0)	12 (11.8)	763 (13.3)
2015	68 (13.3)	190 (13.3)	146 (13.9)	150 (15.5)	62 (12.2)	123 (12.2)	24 (15.2)	7 (6.9)	770 (13.4)
ROP, n (%)	194 (38.0)	522 (36.7)	364 (34.6)	162 (16.7)	160 (31.4)	321 (31.8)	75 (47.5)	31 (30.4)	1829 (31.9)
ROP level									
0	317 (62.0)	902 (63.3)	689 (65.4)	806 (83.3)	350 (68.6)	687 (68.2)	83 (52.5)	71 (69.6)	3905 (68.1)
1	53 (10.4)	163 (11.4)	86 (8.2)	62 (6.4)	61 (12.0)	86 (8.5)	24 (15.2)	9 (8.8)	544 (9.5)
2	66 (12.9)	179 (12.6)	122 (11.6)	54 (5.6)	60 (11.8)	142 (14.1)	33 (20.9)	10 (9.8)	666 (11.6)
3	74 (14.5)	169 (11.9)	154 (14.6)	45 (4.6)	35 (6.9)	91 (9.0)	17 (10.8)	12 (11.8)	597 (10.4)
4	1 (0.2)	5 (0.4)	0 (0.0)	1 (0.1)	2 (0.4)	1 (0.1)	1 (0.6)	0 (0.0)	11 (0.2)
5	0 (0.0)	6 (0.4)	2 (0.2)	0 (0.0)	2 (0.4)	1 (0.1)	0 (0.0)	0 (0.0)	11 (0.2)
Treated ROP, n (%)	32 (6.3)	90 (6.3)	91 (8.6)	33 (3.4)	23 (4.5)	42 (4.2)	13 (8.2)	5 (4.9)	329 (5.7)

GA = gestational age, ROP = retinopathy of prematurity.

for multiplicity has been performed, and the p-values should be considered as exploratory rather than confirmatory. All statistical tests were performed using R version 3.3.2 (open source).

Results

Altogether, 6891 infants had been screened for ROP and registered in SWEDROP between 1.1.2008 and 31.12.2015. During this study period, there were 1157 screened infants with a GA of 31 weeks or more, and 5734 infants with a GA ≤30 weeks – the latter constituting the final study population (Table 1). Comparison with the SNQ register revealed another 40 infants with a GA <31 weeks (40/5774 = 0.7%), who had not been referred for ROP screening.

Among the screened infants, 54.6% (3132/5734) were boys.

Of the total study group, 31.9% (1829/5734) of the infants had ROP, and 5.7% (329/5734) had been treated for ROP. Background data regarding the stages and treatment of ROP, GA (w) and BW (g) during the 8-year study period are presented in Table 1.

Linear regression analyses revealed significant reductions of GA and BW over time of the total study group [5734 infants; OR: −0.028 (CI: −0.051 to −0.004), p = 0.02/OR: −0.053, (CI: −0.093 to −0.014), p = 0.008, respectively]. For illustration of the proportion of GA over time of the total study cohort and of the treated infants, see Fig. 1A,B.

A logistic regression analysis revealed a significantly increased incidence of ROP over the 8-year study period [OR: 1.04 (CI: 1.01–1.06) p = 0.003]. After adjustment for GA and BW, a borderline increase was still present [OR: 1.03 (CI: 1.00–1.06) p = 0.057]. There was no significant increase in the frequency of severe ROP or treated ROP.

Regional data of the study population were available for 5632 of the 5734 infants (98.2%). The number of infants screened for ROP in the seven healthcare regions (1–7), ranged between 158 and 1424 during the total study period (see Table 2).

Overall, the incidence of ROP and the frequency of treatment during the total study period differed between the different regions (p < 0.001). Region 3 had the highest frequency (8.6%), and Region 4 had the lowest total frequency (3.4%) of infants who had been treated for ROP.

There was no overall difference regarding GA and BW between the different regions. Region 2 was the only region with significantly reduced GA (p = 0.004) and BW (p = 0.001) over the 8-year period.

Logistic regression analyses regarding proportion of infants with ROP in the different regions, revealed an increased incidence in regions 2, 3 and 5, see Table 3. After adjustment for GA and BW, the increased incidence remained significant only in regions 3 and 5.

Logistic regression analyses of the proportion of infants treated for ROP in the different regions revealed a significantly increased frequency of treated ROP in one region (Region 3), see Table 3. After adjustment for GA and BW, this significance disappeared, while the proportion of treated infants was reduced in one region (6) and increased in another region (7) – the latter having only 13 treated infants during the total study period.

When analysing the proportion of infants treated for ROP during the year 2015, as compared to the years before the new oxygen routines (2008–2013), the proportion of infants treated for ROP after adjustment for GA and BW, had increased in two regions [Region 3 significantly, OR: 2.24 (CI: 1.11–4.49) p = 0.024, and Region 5 borderline, OR: 3.08 (CI: 0.99–9.60) p = 0.052]. Figure 2A,B,C illustrate the number of treated infants nationwide during 2015, as compared to the previous study

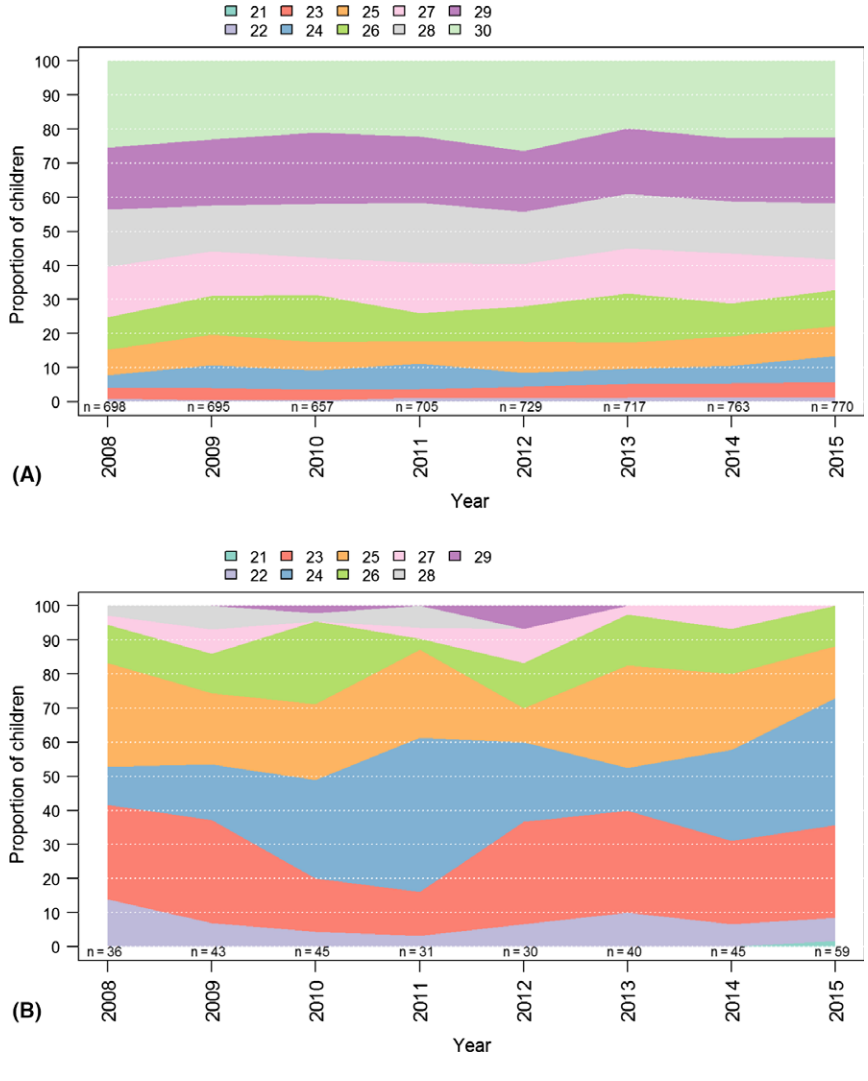

Fig. 1. Proportion of gestational ages (coloured areas represent gestational week at birth) of the total study population of 5734 infants (A) and of the 329 infants treated for retinopathy of prematurity (B) during the study period 2008–2015.

Table 3. Proportion of infants with any retinopathy of prematurity (ROP) and with treated ROP in the seven health care regions in Sweden, including odds ratios (OR) with 95% confidence interval (CI) for the change over the years, before and after adjustment for gestational age (GA) and birthweight (BW).

	Year								Unadjusted		Adjusted for GA and BW	
Region	2008	2009	2010	2011	2012	2013	2014	2015	OR (95% CI)	p-value for slope	OR (95% CI)	p-value for slope
ROP (%)												
Region 1	42	37	42	35	46	31	40	31	0.96 (0.89–1.04)	0.297	0.94 (0.85–1.04)	0.243
Region 2	27	38	33	36	31	41	40	45	1.08 (1.03–1.13)	0.002	1.05 (0.98–1.11)	0.167
Region 3	29	32	29	34	33	38	34	44	1.07 (1.02–1.13)	0.011	1.10 (1.02–1.18)	0.012
Region 4	16	19	22	17	14	18	15	15	0.97 (0.90–1.04)	0.391	0.97 (0.89–1.06)	0.542
Region 5	17	24	30	27	36	43	32	45	1.18 (1.08–1.28)	<0.001	1.20 (1.08–1.32)	<0.001
Region 6	26	43	31	29	28	21	38	40	1.02 (0.96–1.08)	0.479	1.02 (0.94–1.09)	0.682
Region 7	54	50	38	40	42	53	53	46	0.99 (0.87–1.12)	0.837	0.92 (0.78–1.08)	0.296
Total	27	35	31	30	30	32	33	37	1.04 (1.01–1.06)	0.003	1.03 (1.00–1.06)	0.057
Treated ROP (%)												
Region 1	6.5	9.5	10.8	1.8	5.6	6.9	5.3	2.9	0.89 (0.76–1.04)	0.148	0.88 (0.74–1.06)	0.176
Region 2	7	5.2	7.6	5.2	3.7	5.4	7.6	8.9	1.04 (0.95–1.14)	0.402	0.96 (0.86–1.07)	0.440
Region 3	7.9	4.2	5.9	11.5	6.5	9	8.2	14.4	1.11 (1.01–1.22)	0.030	1.10 (0.98–1.23)	0.115
Region 4	2.6	4.8	8.2	2.4	3	3.8	2.9	2	0.92 (0.80–1.07)	0.296	0.92 (0.77–1.08)	0.306
Region 5	2.6	3.7	6	1.7	4	1.9	4.8	11.3	1.18 (0.97–1.42)	0.091	1.06 (0.85–1.31)	0.616
Region 6	4.3	9.6	5.1	2.1	1.7	3.1	4.7	3.3	0.90 (0.78–1.03)	0.123	0.80 (0.68–0.95)	0.011
Region 7	0	10	0	0	12.5	15.8	10.5	12.5	1.28 (0.98–1.67)	0.074	1.48 (1.02–2.13)	0.038
Total	5.2	6.2	6.8	4.4	4.1	5.6	5.9	7.7	1.03 (0.98–1.08)	0.243	1.00 (0.94–1.05)	0.859

period of 2008–2013, and in the two regions with an increased frequency of treatment.

Discussion

The present study encompassing 8 years of infants screened for ROP in Sweden, reports a slightly increased national incidence of ROP during these years, but no significant increase in the frequency of treatment – even when adjusted for GA and BW. Analyses of regional data revealed differences in the country both for incidence of ROP and frequency of infants needing treatment. In accordance with previous reports from SWEDROP (Holmström et al. 2012, 2015, 2016), the national coverage of the register is high and, in the present study, 99.3% of all prematurely born infants in the country with a GA of <31 weeks had been screened for ROP during the 8-year period, thus making the results reliable.

There were slight overall reductions of GA and BW during the study period. When looking at the GA at birth of the treated infants (Fig. 1B), there was an increase of treated infants born in the earliest GA <24 w. In a previous Swedish study of extremely preterm infants born before 27 weeks gestation, a high incidence (73%) of ROP and a high frequency of treatment (20%) were reported (Austeng et al. 2009). With a continuous increase in the survival of the most immature infants, there is a risk of further increasing the incidence of ROP and the frequency of treatment for ROP throughout the country.

Guidelines for ROP screening in Sweden include all infants born before GA 31 weeks, and recommend that neonatologists also refer severely diseased infants above this age (Holmström et al. 2012). In the present study, another 1157 infants with GA of more than 30 weeks had been referred for ROP screening. Only one of these infants had severe ROP and was treated for the ROP. This infant was born 2015 with GA 31 w, was extremely ill, had required high levels of oxygen and was therefore referred for ROP screening by the neonatologist. Such cases are difficult to predict, but emphasize the importance of encouraging neonatologists to refer very sick infants with long periods of high and/or fluctuating levels of oxygen, for ROP screening.

Despite uniform neonatal care and ROP screening routines throughout the country, the present study revealed regional differences in the incidence of ROP and frequency of treatment during the study period. The incidence of ROP ranged from 16.7% (Region 4) to 47.5% (Region 7), and the frequency of treatment from 3.4% (Region 4) to 8.6% (Region 3). The results of Region 7, however, must be interpreted with caution because of the small number of infants.

The incidence of ROP increased over the years in three regions (Regions 2, 3, 5) and the frequency of treatment increased in one region (Region 3). After adjustment for GA and BW, however, increased incidence of ROP remained in only two of the regions (regions 3 and 5), while the increased frequency of treatment in Region 3 was no longer significant. These results accord with the EXPRESS Study, reporting on regional differences in screening for ROP within the study population, which included infants with a GA of <27 weeks born in SWEDEN during 2004–2007 (Austeng et al. 2014). That study reported reduced regional differences with increasing severity of ROP and suspected interobserver bias regarding milder stages of the ROP – a fact that was also discussed by Darlow et al. (2008) in a study on variations between centres in Australia and New Zealand. Differences in indication for treatment must also be considered (Slidsborg et al. 2012). In Sweden, however, the ETROP recommendations for treatment were established already in 2003, before the EXPRESS study was initiated, and are continuously

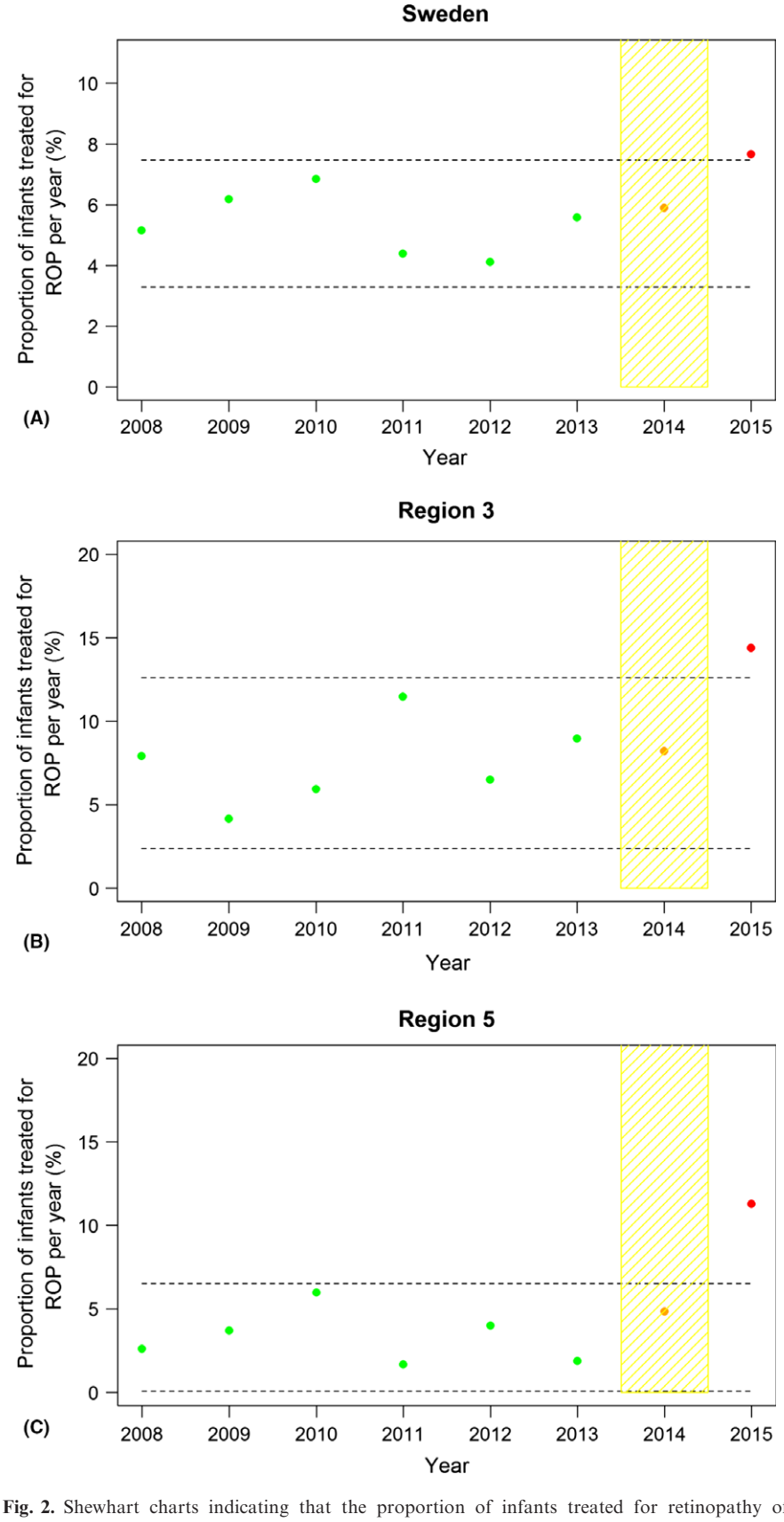

Fig. 2. Shewhart charts indicating that the proportion of infants treated for retinopathy of prematurity (ROP) during 2015 is higher than expected in Sweden (A), in Region 3 (B) and in Region 5 (C). Dotted lines indicate levels for a variation of ±2 standard deviations. Yellow area shows the year 2014 when new oxygen targets were implemented.

highlighted at annual SWEDROP user meetings.

Variations in rates of ROP in high-income countries have been explained by differences in neonatal care, such as different oxygen targets and different routines of monitoring oxygen levels (Darlow et al. 2005). In Sweden, new routines aimed at increased levels of oxygen from previously 88–92% to 91–95% were implemented in most parts of Sweden during 2014. Analyses of the proportion of infants treated for ROP in 2015 in the different healthcare regions, as compared to the years before the new oxygen routines (2008–2013) revealed that the frequency of treatment for ROP had increased in two regions and nearly doubled in one region (Region 3). The frequency did not increase in one region (Region 6), which did not implement the new oxygen routines. Our finding accords with a recent study from Australia that reported increased incidence and severity of ROP after changing oxygen targets from 88–92% to 91–95% (Manley et al. 2016). It may be speculated that the differences within Sweden can be explained by differences in monitoring of oxygen levels and compliance with saturation targets. This was, however, not investigated in the present study.

Conclusion

The present study revealed a slightly increased national incidence of ROP in Sweden over the 8-year study period, and regional differences with higher frequencies of infants with treated ROP in two regions. Changing oxygen target saturation limits may explain this finding. The impact of these factors on ROP development is investigated in an ongoing study.

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