COMPARISON OF ADMISSION RATES TO NEONATAL UNITS BETWEEN PULSE OXIMETRY SCREENING AND NON-PULSE OXIMETRY SCREENING UNITS

STATISTICAL REPORT

Version 0.1

6th July 2017

Written By: Date:	Sena Jawad Neonatal Clinical Trials Statistician Department of Academic Neonatal Medicine Imperial College London 06/07/2017
Reviewed By: Date:	Dr Chis Gale Clinical Senior Lecturer in Neonatal Medicine Department of Academic Neonatal Medicine Imperial College London 07/07/2017
Approved By: Date:	Professor Andrew Ewer

TABLE OF CONTENTS

TABLES

1 STUDY SUMMARY

TITLE	Comparison of admission rates to neonatal units between PO screening and non-PO screening Units
DESIGN	Register-based epidemiological study using anonymised data
AIMS	To determine the effect of introducing pulse oximetry screening on admission rates to neonatal units
OUTCOME MEASURES	Primary: admission to neonatal unit and the cost implications
POPULATION	Infants born in match neonatal units in England.
ELIGIBILITY	All infants >34 weeks gestation who were admitted unexpectedly to matched neonatal units over a specified time period, who are registered in the National Neonatal Research Database (NNRD).
DURATION	Retrospective, non-identifiable data held in a pre-existing research database (the NNRD) on infants born between 2015 and 2016 will be used.

2 BACKGROUND

A parallel study will collect essential data for the scenario that would exist in the absence of screening. It will explore the outcome for these infants had they not received pulse oximetry screening for either CCHD alone, or CCHD and Other Significant Non Cardiac Related Serious Illnesses, will be determined from. In this parallel, but essential complimentary study, data will be accessed by the Neonatal Data Analysis Unit (NDAU) which has access to the BADGER database. All Neonatal Units in the UK feed their data into a data collection system known as BADGER which can be fully accessed by NDAU. The particular data of interest here will relate to the babies who reach term but have unexpected admissions (Term Unexpected Admissions). Ewer and colleagues have already conducted a pilot study to ascertain clinical impact of PO screening for CCHD and other non-cardiac related illness, in the six months from June to December 2015. Through NDAU, data will be accessed for outcomes of babies in both the pilot sites and non-pilot sites for this period. First, this parallel study will take the approach of identifying and extracting the data for neonatal centres that participated in the pilot study. It is anticipated infant outcome (Term Unexpected Admissions) data will be collected for 12 months in total, but for six months prior to the pilot study and the 6 months during the pilot study that introduced PO screening for the combined targeted conditions. This will show the impact of introducing PO screening for the combined targeted condition over the 12 months. Data will also be collected for matched group of centres which did not participate in the pilot study for the same 12 months. Outcomes for babies in the pilot and the non-pilot study will be assessed also at 6 months and 12 month after the pilot study's end date to compare whether infants detected by a positive pulse oximetry test have outcomes which are different to babies who were not subject to screening. From this analysis we will estimate the probability that screening for CCHD alone, or CCHD and other serious conditions, will truly detect early cases of serious complications that would otherwise be missed in the absence of PO screening. Thus this parallel study will provide essential data for the comparator 'No PO Screening' arm of the model.

3 STATISTICAL METHODS

Segmented linear regression models, a type of interrupted time series model, were used to model the effect of the screening program to test for a difference in the post-screening trend compared to the pre-screening period. The screening intervention was rolled out in July 2015 and took approximately 6 months, until December 2015 to be fully implemented. Therefore segmented linear regression was used to estimate a step change and a trend change in the year before and the year following the screening intervention. Regression estimates of the pre-intervention trend, post-estimated trend (adjusted for the pre-intervention period) and the step change after the intervention were calculated with corresponding 95% confidence intervals and p-values. Autocorrelations were explored and assessed using residual plots with the Breusch-Godfrey test. Adjusted analyses were conducted to explore the possible confounding effects of birth weight and gestational age, however all analyses were conducted on a unit-level rather than the infant level. Sensitivity analyses were conducted to explore the screening effect without including units who had implemented a form of the screening intervention before the study intervention. No adjustments for multiple testing were explored. All analysis was conducted using STATA 14 and SAS 9.4.

4 RESULTS

4.1 Summary Statistics

4.1.1 BASELINE CHARACTERISTICS

	Pulse Oximetry (n=21,175)		Matched Controls (n=20,226)		P-value for difference†
Gestational age (weeks^{+days}), n (%)					P<0.001
<37^{+0}	4,933	(23.3%)	3,945	(19.5%)	
≥37^{+0}	16,241	(76.7%)	16,279	(80.5%)	
Birth weight (g), mean (SD)	3149.1	(692.9)	3216.9	(663.9)	P<0.001
Missing	*0*	*(0%)*	*2*	*(0.01%)*	

† P-values from chi-squared tests or t-tests

Table 1 Summary of baseline characteristics

4.1.2 BI-ANNUAL RESPIRATORY AND SEPSIS ADMISSIONS

Table 2 **Summary of bi-annual respiratory and sepsis admissions**

	n respiratory and sepsis admissions / total admissions (%)					
	Jul – Dec 2014	**Jan – Jun 2015**	**Jul – Dec 2015**	**Jan – Jun 2016**	**Jul – Dec 2016**	**All**
Pulse Oximetry	2,346/3,922 (59.8%)	2,390/3,891 (61.4%)	2,612/4,237 (61.7%)	2,745/4,341 (63.2%)	2,968/4,784 (62.04%)	13,061/21,175 (61.7%)
Matched Controls	1,902/3,929 (48.4%)	2,001/3,906 (51.23%)	2,084/4,014 (51.9%)	2,131/4,101 (52.0%)	2,166/4,276 (50.7%)	10,284/20,226 (50.9%)

4.2 Respiratory and Sepsis Admissions

Table 3 **Segmented Regression Results for Respiratory and Sepsis Admissions as a Percentage of All Admissions**

Respiratory and sepsis admissions (% of total admissions)	**Estimate**	**SE**	**P-value**	**95% CI**
Pulse Oximetry Group				
Pre-intervention trend (monthly increase in % admissions)	0.25	0.25	0.33	-0.27 to 0.78
Post-intervention trend adjusted for pre-intervention (monthly increase in % admissions)	-0.09	0.23	0.71	-0.57 to 0.40
Step change (increase in % admissions at Jan 2016)	-0.35	3.48	0.92	-7.62 to 6.92
Trend change (difference in pre and post intervention trend)	-0.34	0.34	0.33	-1.06 to 0.37
Matched Controls Group				
Pre-intervention trend (monthly increase in % admissions)	0.47	0.23	0.05	-0.00 to 0.94
Post-intervention trend accounting for pre-intervention (monthly increase in % admissions)	-0.28	0.22	0.22	-0.75 to 0.18
Step change (increase in % admissions at Jan 2016)	-2.06	3.17	0.52	-8.67 to 4.55
Trend change (difference in pre and post intervention trend)	-0.75	0.32	0.03	-1.41 to -0.09

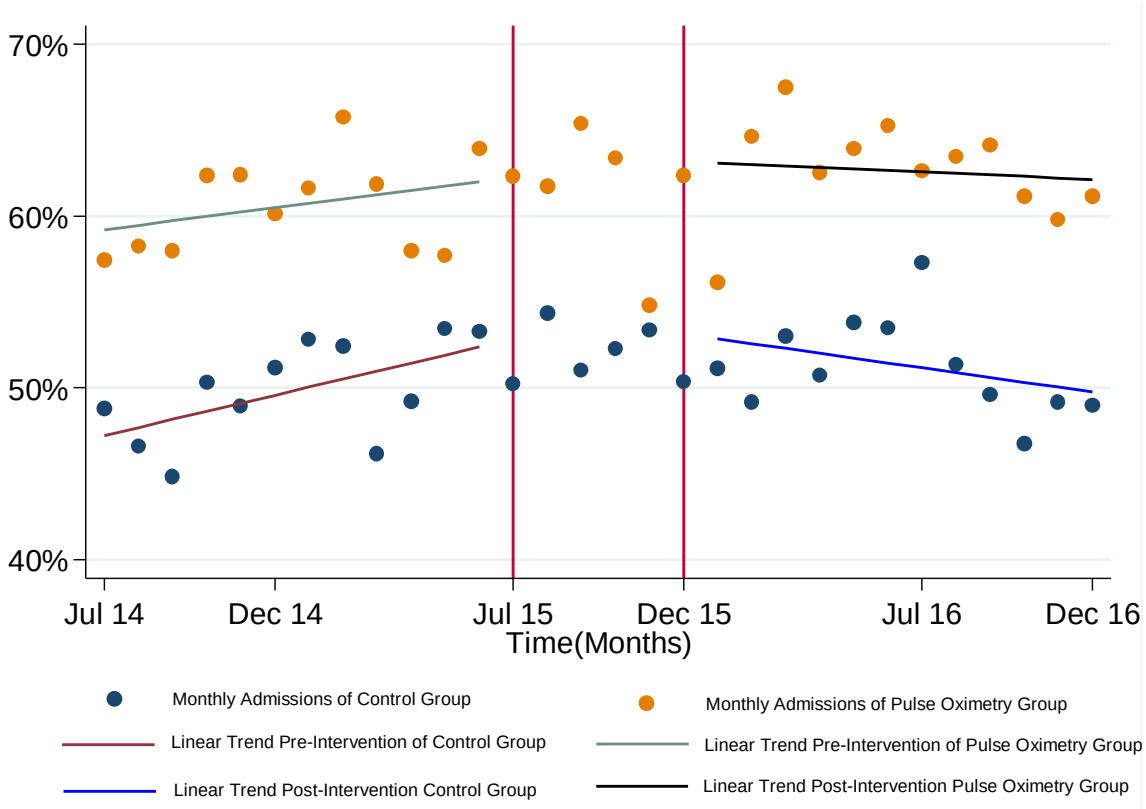

Figure 1 Monthly respiratory and sepsis admissions as a percentage of all monthly admissions by screening arm. The red vertical lines indicate the screening roll-out period. Linear trend lines use post-estimations from segmented linear regression models

Table 4 Segmented Regression Results for the Number of Respiratory and Sepsis Admissions

Respiratory and sepsis admissions (number of admissions)	Estimate	SE	P-value	95% CI
Pulse Oximetry Group				
Pre-intervention trend (monthly increase in admissions)	1.92	2.35	0.42	-2.98 to 6.83
Post-intervention trend adjusted for pre-intervention (monthly increase in admissions)	5.02	2.18	0.03	0.48 to 9.56
Step change (increase in admissions at Jan 2016)	26.59	32.56	0.42	-41.32 to 94.50
Trend change (difference in pre and post intervention trend)	3.10	3.20	0.35	-3.59 to 9.78
Matched Controls Group				
Pre-intervention trend (monthly increase in admissions)	3.73	2.65	0.18	-1.81 to 9.26
Post-intervention trend accounting for pre-intervention (monthly increase in admissions)	-0.74	2.63	0.78	-6.22 to 4.74
Step change (increase in admissions at Jan 2016)	-4.18	37.28	0.91	-81.93 to 73.58
Trend change (difference in pre and post intervention trend)	-4.47	3.73	0.25	-12.26 to 3.32

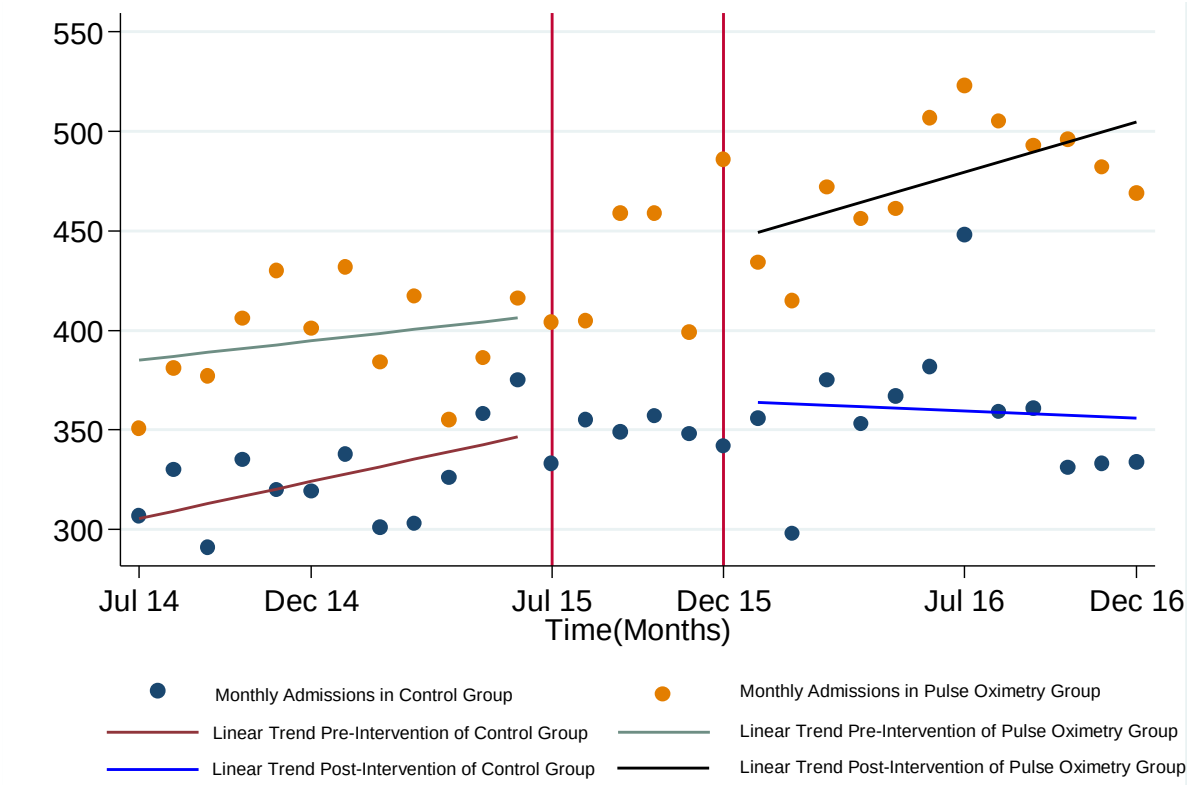

Figure 2 **Monthly respiratory and sepsis admissions by screening arm. The red vertical lines indicate the screening roll-out period. Linear trend lines use post-estimations from segmented linear regression models.**

4.3 Length of Care Stay

Table 5 **Segmented Regression Results for the Mean Length of Stay in Days**

Length of stay (mean days)	Estimate	SE	P-value	95% CI
Pulse Oximetry Group				
Pre-intervention trend (monthly mean increase in length of stay)	-0.03	0.02	0.12	-0.07 to 0.01
Post-intervention trend adjusted for pre-intervention (monthly mean increase in length of stay)	-0.03	0.02	0.06	-0.07 to 0.001
Step change (increase in mean length of stay at Jan 2016)	0.10	0.26	0.71	-0.44 to 0.64
Trend change (difference in pre and post intervention trend)	-0.004	0.03	0.88	-0.06 to 0.05
Matched Controls Group				
Pre-intervention trend (monthly mean increase in length of stay)	0.04	0.02	0.06	-0.001 to 0.09
Post-intervention trend adjusted for pre-intervention (monthly mean increase in length of stay)	-0.03	0.02	0.11	-0.08 to 0.01
Step change (increase in mean length of stay at Jan 2016)	-0.50	0.30	0.11	-1.12 to 0.13
Trend change (difference in pre and post intervention trend)	-0.08	0.03	0.02	-0.14 to -0.02

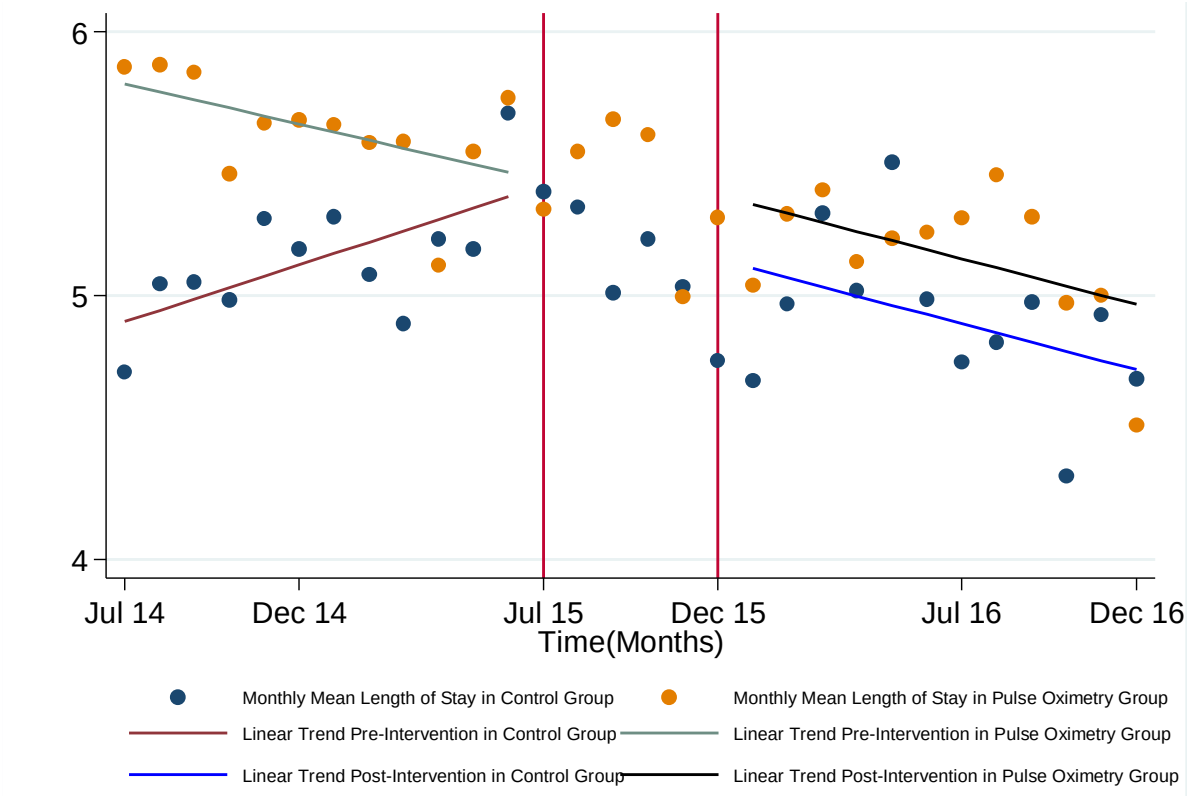

Figure 3 **Monthly mean length of stay on unit by screening arm. The red vertical lines indicate the screening roll-out period. Linear trend lines use post-estimations from segmented linear regression models.**

Table 6 Segmented Regression Results for the Mean Length of Stay in Days Stratified by Level of Care

Length of stay (mean days)	Estimate	SE	P-value	95% CI
Pulse Oximetry Group				
Intensive Care				
Pre-intervention trend (monthly mean increase in length of stay)	-0.09	0.07	0.21	-0.22 to 0.05
Post-intervention trend adjusted for pre-intervention (monthly mean increase in length of stay)	0.03	0.07	0.71	-0.12 to 0.17
Step change (increase in mean length of stay at Jan 2016)	0.95	0.95	0.33	-1.04 to 2.94
Trend change (difference in pre and post intervention trend)	0.11	0.10	0.26	-0.09 to 0.31
High Dependency				
Pre-intervention trend (monthly mean increase in length of stay)	-0.003	0.05	0.94	-0.10 to 0.10
Post-intervention trend adjusted for pre-intervention (monthly mean increase in length of stay)	-0.12	0.05	0.01	-0.22 to -0.03
Step change (increase in mean length of stay at Jan 2016)	0.91	0.66	0.19	-0.48 to 2.29
Trend change (difference in pre and post intervention trend)	-0.12	0.07	0.09	-0.26 to 0.02
Special Care				
Pre-intervention trend (monthly mean increase in length of stay)	-0.03	0.01	0.09	-0.06 to 0.004
Post-intervention trend adjusted for pre-intervention (monthly mean increase in length of stay)	-0.02	0.01	0.19	-0.05 to 0.01
Step change (increase in mean length of stay at Jan 2016)	0.11	0.20	0.59	-0.31 to 0.52
Trend change (difference in pre and post intervention trend)	0.01	0.02	0.72	-0.03 to 0.05
Matched Controls Group				
Intensive Care				
Pre-intervention trend (monthly mean increase in length of stay)	0.11	0.06	0.06	-0.01 to 0.23
Post-intervention trend adjusted for pre-intervention (monthly mean increase in length of stay)	-0.04	0.06	0.52	-0.16 to 0.08
Step change (increase in mean length of stay at Jan 2016)	-0.55	0.79	0.50	-2.21 to 1.11
Trend change (difference in pre and post intervention trend)	-0.15	0.08	0.08	-0.32 to 0.02
High Dependency				
Pre-intervention trend (monthly mean increase in length of stay)	0.16	0.05	0.01	0.05 to 0.27
Post-intervention trend adjusted for pre-intervention (monthly mean increase in length of stay)	-0.02	0.05	0.74	-0.12 to 0.09
Step change (increase in mean length of stay at Jan 2016)	-2.00	0.73	0.01	-3.51 to -0.49
Trend change (difference in pre and post intervention trend)	-0.18	0.07	0.02	-0.33 to -0.03
Special Care				

Pre-intervention trend (monthly mean increase in length of stay)	-0.004	0.01	0.71	-0.03 to 0.02
Post-intervention trend adjusted for pre-intervention (monthly mean increase in length of stay)	-0.02	0.01	0.20	-0.04 to 0.01
Step change (increase in mean length of stay at Jan 2016)	0.05	0.16	0.78	-0.29 to 0.39
Trend change (difference in pre and post intervention trend)	-0.01	0.02	0.49	-0.05 to 0.02

5 SENSITIVITY ANALYSIS

5.1 Adjusted Analysis

Table 7 Segmented Regression Results for Respiratory and Sepsis Admissions as a Percentage of

Respiratory and sepsis admissions (% of total admissions)	Estimate	SE	P-value	95% CI
Pulse Oximetry Group				
Pre-intervention trend (monthly increase in % admissions)	0.29	0.27	0.30	-0.27 to 0.85
Post-intervention trend adjusted for pre-intervention (monthly increase in % admissions)	-0.14	0.26	0.60	-0.68 to 0.40
Step change (increase in % admissions at Jan 2016)	-0.48	3.80	0.90	-8.46 to 7.49
Trend change (difference in pre and post intervention trend)	-0.43	0.39	0.29	-1.24 to 0.39
Matched Controls Group				
Pre-intervention trend (monthly increase in % admissions)	0.48	0.24	0.06	-0.03 to 0.98
Post-intervention trend accounting for pre-intervention (monthly increase in % admissions)	-0.21	0.24	0.38	-0.71 to 0.29

All Admissions Adjusted for Birth weight and Gestational Age

Step change (increase in % admissions at Jan 2016)	-3.07	3.54	0.40	-10.51 to 4.38
Trend change (difference in pre and post intervention trend)	-0.69	0.32	0.04	-1.36 to -0.02

Table 8 Segmented Regression Results for the Number of Respiratory and Sepsis Admissions Adjusted for Birth weight and Gestational Age

Respiratory and sepsis admissions (number of admissions)	Estimate	SE	P-value	95% CI
Pulse Oximetry Group				
Pre-intervention trend (monthly increase in admissions)	2.26	2.49	0.38	-2.98 to 7.51
Post-intervention trend adjusted for pre-intervention (monthly increase in admissions)	4.53	2.40	0.08	-0.51 to 9.57
Step change (increase in admissions at Jan 2016)	17.00	35.43	0.64	-57.43 to 91.43
Trend change (difference in pre and post intervention trend)	2.26	3.60	0.54	-5.30 to 9.83
Matched Controls Group				
Pre-intervention trend (monthly increase in admissions)	5.13	2.79	0.08	-0.73 to 10.99
Post-intervention trend accounting for pre-intervention (monthly increase in admissions)	0.98	2.75	0.73	-4.79 to 6.75
Step change (increase in admissions at Jan 2016)	-35.53	40.94	0.40	-121.54 to 50.48
Trend change (difference in pre and post intervention trend)	-4.15	3.66	0.27	-11.84 to 3.55

5.2 Respiratory and Sepsis Admissions

Table 9 Segmented Regression Results for Respiratory and Sepsis Admissions as a Percentage

Respiratory and sepsis admissions (% of total admissions)	Estimate	SE	P-value	95% CI
Pulse Oximetry Group (n=10,459)				

of All Admissions excluding units who implemented screening before the pilot study

Pre-intervention trend (monthly increase in % admissions)	0.73	0.31	0.03	0.08 to 1.37
Post-intervention trend adjusted for pre-intervention (monthly increase in % admissions)	0.43	0.29	0.15	-0.17 to 1.03
Step change (increase in % admissions at Jan 2016)	-4.13	4.27	0.34	-13.03 to 4.77
Trend change (difference in pre and post intervention trend)	-0.29	0.42	0.49	-1.17 to 0.58
Matched Controls Group (n=20,226)				
Pre-intervention trend (monthly increase in % admissions)	0.47	0.23	0.05	-0.001 to 0.94
Post-intervention trend accounting for pre-intervention (monthly increase in % admissions)	-0.28	0.22	0.22	-0.75 to 0.18
Step change (increase in % admissions at Jan 2016)	-2.06	3.17	0.52	-8.67 to 4.55
Trend change (difference in pre and post intervention trend)	-0.75	0.32	0.03	-1.41 to -0.09

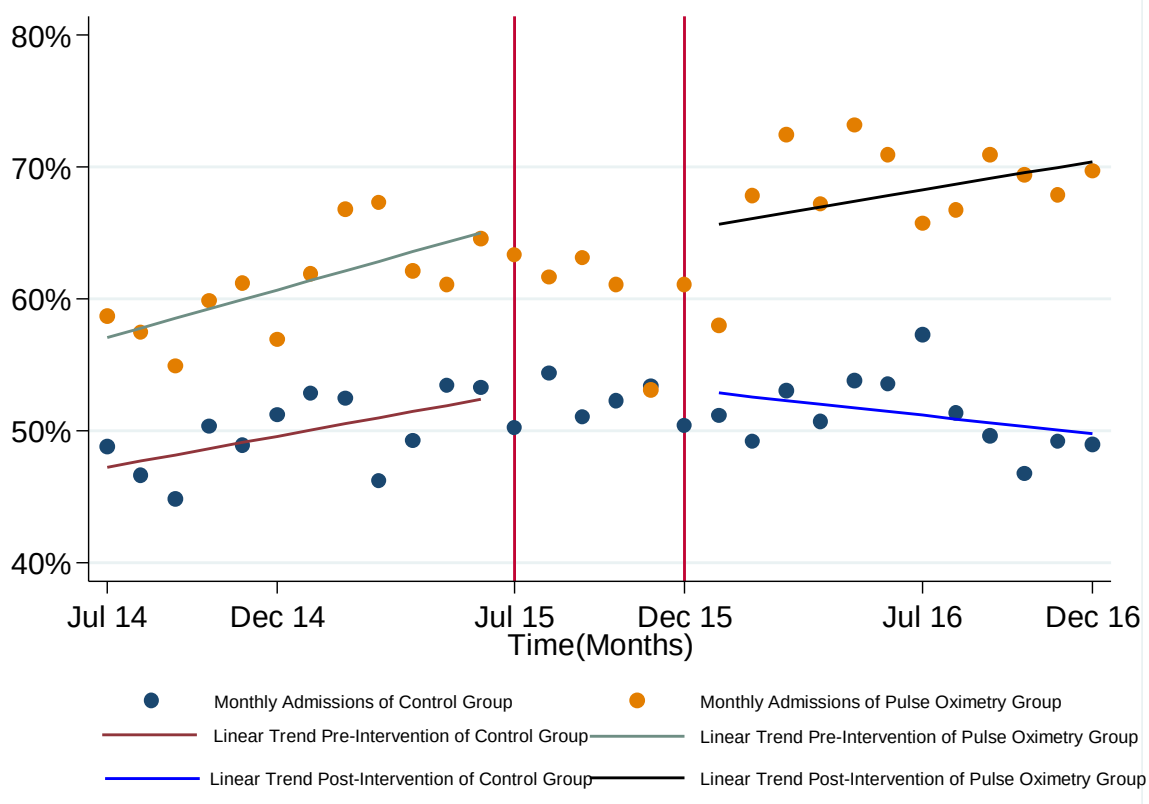

Figure 4 Monthly respiratory and sepsis admissions as a percentage of all monthly admissions by screening arm, excluding units who implemented the screening before the pilot study. The red vertical lines indicate the screening roll-out period. Linear trend lines use post-estimations from segmented linear regressions models.

Table 10 Segmented Regression Results for the Number of Respiratory and Sepsis Admissions excluding units who implemented screening before the pilot study

Respiratory and sepsis admissions (number of admissions)	Estimate	SE	P-value	95% CI

Pulse Oximetry Group				
Pre-intervention trend (monthly increase in admissions)	2.46	1.48	0.11	-0.63 to 5.56
Post-intervention trend adjusted for pre-intervention (monthly increase in admissions)	2.03	1.38	0.16	-0.85 to 4.91
Step change (increase in admissions at Jan 2016)	11.91	20.50	0.57	-30.86 to 54.68
Trend change (difference in pre and post intervention trend)	-0.43	2.03	0.83	-4.66 to 3.79
Matched Controls Group				
Pre-intervention trend (monthly increase in admissions)	3.73	2.65	0.18	-1.81 to 9.26
Post-intervention trend accounting for pre-intervention (monthly increase in admissions)	-0.74	2.63	0.78	-6.22 to 4.74
Step change (increase in admissions at Jan 2016)	-4.18	37.28	0.91	-81.93 to 73.58
Trend change (difference in pre and post intervention trend)	-4.47	3.73	0.25	-12.26 to 3.33

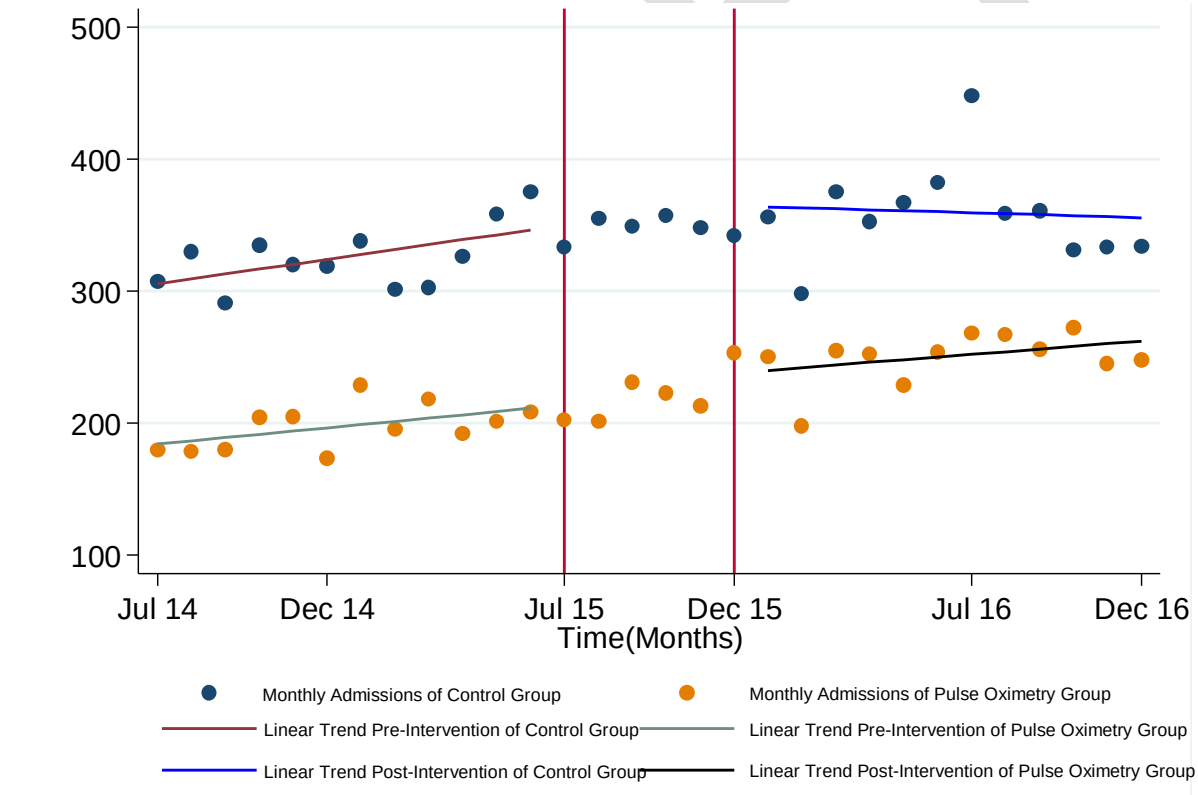

Figure 5 **Monthly respiratory and sepsis admissions by screening arm, excluding units who implemented the screening before the pilot study. The red vertical lines indicate the screening roll-out period. Linear trend lines use post-estimations from segmented linear regression models.**

Table 11 Segmented Regression Results for the Mean Length of Stay in Days excluding units who implemented screening before the pilot study

Length of stay (mean days)	Estimate	SE	P-value	95% CI
Pulse Oximetry Group				
Pre-intervention trend (monthly mean increase in length of stay)	-0.03	0.03	0.22	-0.09 to 0.02
Post-intervention trend adjusted for pre-intervention (monthly mean increase in length of stay)	-0.003	0.03	0.91	-0.06 to 0.05
Step change (increase in mean length of stay at Jan 2016)	-0.12	0.38	0.76	-0.90 to 0.67
Trend change (difference in pre and post intervention trend)	0.03	0.04	0.41	-0.05 to 0.11
Matched Controls Group				
Pre-intervention trend (monthly mean increase in length of stay)	0.04	0.02	0.06	-0.001 to 0.09
Post-intervention trend adjusted for pre-intervention (monthly mean increase in length of stay)	-0.03	0.02	0.11	-0.08 to 0.01
Step change (increase in mean length of stay at Jan 2016)	-0.50	0.30	0.11	-1.12 to 0.13
Trend change (difference in pre and post intervention trend)	-0.08	0.03	0.02	-0.14 to -0.02

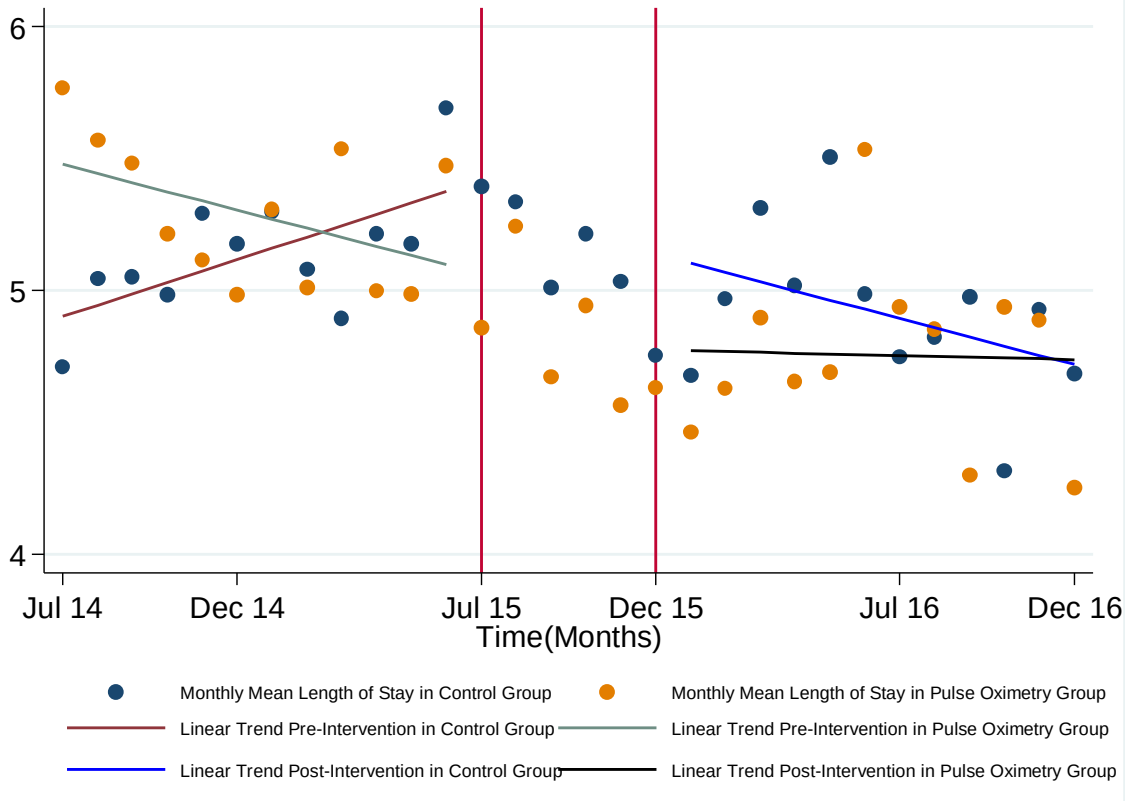

Figure 6 Monthly mean length of stay on unit by screening arm, excluding units who implemented the screening before the pilot study. The red vertical lines indicate the screening roll-out period. Linear trend lines use post-estimations from segmented linear regression models.