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Early View

Research letter

Restricted visiting reduces nosocomial viral respiratory tract infections in high-risk neonates

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Restricted visiting reduces nosocomial viral respiratory tract infections in high-risk neonates

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Take home message

Restricting visitors on the neonatal intensive care unit to parents only during a worldwide pandemic resulted in a 39% reduction in nosocomial viral respiratory tract infections in neonatal patients. These findings need validating in a prospective trial.

Viral respiratory tract infections (VRTIs) are more prevalent in the neonatal intensive care unit (NICU) than previously thought with up to 52% of infants having evidence of viral carriage (1, 2). We, and others, have previously reported nosocomial VRTIs can cause significant morbidity (3), particularly in preterm infants, including escalation of respiratory support, longer hospital stay, increased requirement for home oxygen and greater healthcare costs (1, 4). Viral carriage in the airways of children and adults may have few or no symptoms (3, 5), potentially implicating them as an inadvertent source of nosocomial VRTI when visiting the NICU. During worldwide pandemics, such as the recent H1N1, this could have devastating consequences (3); most VRTI outbreaks on NICUs trigger measures to reduce spread, including visitor restrictions (6, 7). No studies have explored the impact of planned visitor restrictions on NICU nosocomial VRTIs. We aimed to study the impact of planned NICU winter visitor restrictions during the H1N1 pandemic.

This study was carried out using routine electronic patient data from two UK tertiary NICUs, covering the Trent Perinatal Network annual birth population of 26,000, between August 2007 and May 2013. Their combined capacity is 16 intensive care, 8 high dependency and 14 special care cots. The NICUs are part of two large teaching hospitals with 1700 beds providing a population of 4-5 million with all specialist healthcare services including paediatric and adult intensive care. Normal NICU visiting allows 24 hour access for the parents of the baby with a 2-8pm visiting time for family and friends including children. During the period of maximal H1N1 community prevalence in the UK (October to March in 2009/10 and 2010/11), planned visitor restrictions were in place with only parents allowed

aiming to minimise cross-contamination in this high-risk population of babies. The same restrictions were in place during the same winter period of 2011/12 following the second more severe H1N1 winter (8) and the uncertainty of a possible third peak. Throughout the study period identical infection prevention policies were in place in both hospitals including hand hygiene, isolation procedures for infected babies, and staff or visitors with infections were advised to stay away until well. Babies clinically suspected of having a VRTI were isolated and screened, using real-time PCR from respiratory secretions, and declared positive as previously described (4). Babies are not readmitted to the NICU after discharge.

We used a Poisson generalised additive model (GAM) to model the number of cases per two month period as a function of several explanatory variables to estimate an incidence rate ratio (IRR) for changes in the incidence of infection during restrictions. The model included a thin plate spline to capture the underlying temporal trend in the rate of infection, a categorical variable to model seasonal variations in the rate of infection by two month period, plus variables to model NICU workload intensity (operationalised as the percentage of all bed days classed as intensive care) and the number of positive VRTI samples across all hospital inpatients (including hospital acquired infections). The latter two variables were log-transformed to make them more normally distributed. The total number of NICU bed days in each period was used as an offset term in the Poisson model to account for variations in the number of babies at risk of developing infection.

We built a full model containing all potential explanatory variables and then used a backwards fitting approach to build a parsimonious model taking a $p<0.05$ as an indicator of parameter significance. Akaike Information Criterion (AIC) was used to compare alternative

models, examined our model for evidence of over dispersion to ensure the Poisson distribution was appropriate and examined residuals for normality and evidence of remaining autocorrelation.

We used the function 'gam' from the library 'mcgv' in the statistical software R version 3.0.2 to model the data (9). Ethical approval was granted by the University of Nottingham Medical School Ethics Committee.

A total of 6808 respiratory viruses were identified by PCR with no significant differences between 3 monthly positive samples during the restricted winter periods (median 434, IQR 285-582) compared to non-restricted winter periods (median 451, IQR 338-482, p=0.93). In total, 77,313 NICU bed days were delivered (mean 2209 (SD 135) per two month period) with 22.1% (SD 3.7) classed as intensive care. 100 separate VRTI episodes were identified in 95 NICU patients (mean 2.9 cases per two month period, standard deviation SD=2.6) (Table). Rhinovirus accounted for 33% of all patent samples but 73% of neonatal samples. H1N1 peaked in the winter of 2010/11 but only one infant (with ventilator dependent chronic lung disease who died) tested positive during this restriction period.

The results of the GAM models used to estimate the IRR for the change in rate of infection during restriction periods were: parsimonious model IRR 0.61 (95% CI 0.38-0.99, AIC 147.9, adjusted R^2=0.28, p=0.044) which included a thin plate spline for underlying trend and percentage intensive care days; the full model IRR 0.60 (95% CI 0.36-0.99, AIC 149.8, adjusted R^2=0.26, p=0.046) which included the parsimonious model variables and

categorical seasonal variable and total positive VRTI samples. The parsimonious model suggests a 39% reduction in the incidence of infection in the periods when restricted visiting arrangements were in place.

Our study, one of the first to report a planned period of visitor restriction during a worldwide influenza pandemic, suggests stricter NICU visiting practice could reduce nosocomial VRTIs by 39%. These babies have never left the NICU and so probably acquired the infection from visitors or staff, many of whom may have subclinical infection (3, 5). There is significant variability in visiting practices and dealing with outbreaks of VRTIs on the NICU (6, 7) and in other clinical settings (10, 11). Minimising the risks of nosocomial VRTIs could have an impact on neonatal bronchopulmonary dysplasia, length of hospital stay and could reduce the need of home oxygen which is double that of non-infected preterm infants (4). An observational study in a 527 bed tertiary children's hospital demonstrated a similar 37% reduction in nosocomial VRTIs following introduction of a standardised visitation policy although these were not as strict as our study (12). This study, nor the present one, were able to address the impact staff viral carriage could have on nosocomial VRTI.

Using a robust method accounting for underlying temporal and seasonal trends to isolate the intervention is a major strength. Another strength of the modelling approach includes factoring in the population burden, using positive hospital admissions as a crude marker, and NICU workload intensity. No other infection prevention strategies were introduced during this period and the study window includes winter periods before and after planned restrictions. However, the main limitation of our study is the low event rate (VRTI) with

borderline significance although the inclusion of important confounders in the Poisson model is a strength. Other limitations include being based on two centres only and potentially only a small part of the variance has been captured (R^2=0.28). The uptake of antivirals and flu vaccination could not be assessed although these may not have a significant impact between seasons particularly as the H1N1 vaccine programme started after the first peak incidence (13).

Our results raise the possibility that nosocomial acquired VRTI in the NICU can be reduced by visitor restrictions and this could be an important preventative measure during worldwide pandemics (3). These findings need further validation and could also be extended to studies exploring the impact of this policy throughout the year with a focus on reducing bronchopulmonary dysplasia, home oxygen need and healthcare costs whilst minimising the impact on family-centered care and parent wellbeing (14).

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Table: Number of episodes of PCR positive viral respiratory tract infections from inpatients between 2007 to 2013 in two large teaching hospitals in Nottingham, UK. All patient samples (excluding NICU) are shown per quarter with the NICU viruses identified paired below. The shaded areas denote the approximate periods of visiting restrictions to the NICU. Viruses are grouped as follows: Inf=Influenza A, B and C; InfPan=H1N1 pandemic influenza; PF=Parainfluenza 1-4; Rhino=Rhinovirus, RSV=Respiratory syncytial virus, Other=Adenovirus, Cytomegalovirus, Coronavirus, Epstein Barr virus; Herpes Simplex virus; Murine pneumonia virus

		2007		2008				2009				2010				2011				2012				2013		
Virus	**Group**	Aug-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-May	**Total**
Inf	All	3	12	27	15	0	93	16	4	13	12	1	1	0	43	27	0	0	1	44	11	0	69	113	18	**525**
	NICU								**1**															**1**		
InfPan	All	0	0	0	0	0	0	0	0	0	67	10	0	0	118	37	0	0	0	0	0	0	0	0	0	**237**
	NICU										**4**					**1**										
PF	All	16	24	9	41	12	8	32	24	22	17	16	39	5	8	15	28	12	21	17	31	16	24	73	67	**588**
	NICU											**1**					**1**		**1**	**2**	**1**			**5**		
Rhino	All	47	68	68	57	75	107	112	60	78	127	76	97	65	121	126	88	68	147	134	102	80	161	102	97	**2333**
	NICU	**3**	**4**	**1**	**4**		**6**	**1**	**5**	**4**	**1**		**3**	**3**		**1**	**3**	**7**	**2**	**1**	**9**	**1**	**3**	**7**	**1**	
RSV	All	19	237	57	1	11	297	50	6	4	202	55	3	0	218	167	5	0	186	188	8	5	242	112	19	**2098**
	NICU						**1**					**1**								**3**			**1**			
Other	All	12	31	54	26	14	82	94	28	10	26	58	20	4	7	71	20	5	20	82	74	25	76	78	98	**1021**
	NICU							**3**													**1**	**1**	**1**			
Total		**100**	**376**	**216**	**144**	**112**	**594**	**308**	**128**	**131**	**456**	**218**	**163**	**77**	**515**	**445**	**145**	**92**	**378**	**471**	**237**	**128**	**577**	**491**	**300**	**6802**