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**Title:** Evidence of increased pathogenicity of HRVC compared with HRVA and B: Comparisons between children with an acute lower respiratory illness and controls

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**Body:** Introduction: Recent studies suggest that human rhinovirus group C (HRVC) is more pathogenic in young children than HRVA and B. However, the relative frequency of isolation of these HRV groups between children presenting to an emergency department (ED) with an acute lower respiratory illness (ALRI) and healthy community controls has not been determined. Aim: To compare isolation rates for HRVA, B and C between children with an ALRI presenting to ED and health community controls. Methods: Children aged 0-5 years presenting with an ALRI to the ED of a tertiary paediatric hospital along with healthy children from a local childcare centre were prospectively recruited. A nasal sample was collected at recruitment from which RNA was extracted and reverse transcribed. From cDNA, a 2-step PCR of the HRV 5' NCR was used for HRV detection and molecular typing. Results: There were no differences in isolation rates for HRVA between ALRI cases and controls. Isolation rates for HRVB were low and slightly higher in controls than cases. For HRVC, not only were isolation rates higher than for HRVA or B, but rates were substantially higher for cases versus controls (48.5 vs 8.7%,  $p<0.001$ ).

Table 1: Cases versus controls

	cases	controls	p-value
n	167	69	
HRVA (%)	33 (19.8)	12 (17.9)	0.14

HRVB (%)	3 (1.8)	5 (7.2)	0.049
HRVC (%)	81 (48.5)	6 (8.7)	<0.001

Conclusions: HRVC is the most common HRV group causing ALRI in this group of young children, but is relatively uncommon in healthy children. In contrast, HRVA and B were not more common in children with ALRI than controls. These data provide support for HRVC being more pathogenic than HRVA and B.