

Pertussis severity of disease in hospitalised children during an epidemic

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To optimise protection for our children and the community against infectious diseases by ensuring the safety and effectiveness of vaccines and immunisation.

Research Program:

Immunisation practice and policy development in Australia: responding to urgent priorities in prevention of endemic and epidemic infectious diseases in children.



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Pertussis severity study

A cross sectional observational study to describe the clinical severity of pertussis infection and risk factors for severe disease in Australian children hospitalised over a 12 month epidemic period



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Background

Severity of disease in hospitalised children

- Limited data
 - on Australian children hospitalised with a primary diagnosis of pertussis¹
 - Severity of disease in hospitalised children during an epidemic period²

Pertussis severity scoring system

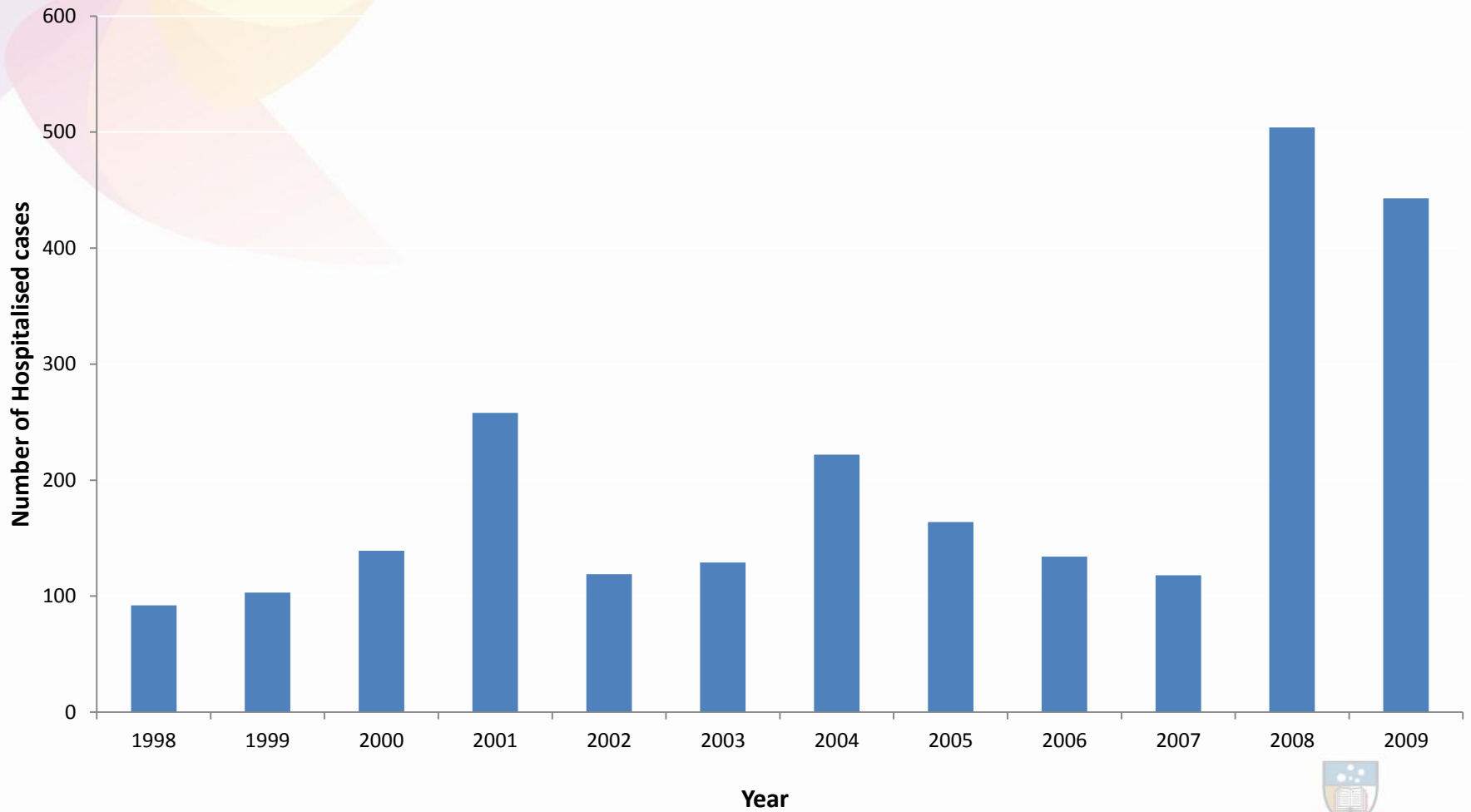
- A clinical scoring system for pertussis based on symptoms of the disease for community cases of pertussis³
- Severity scoring system for RSV “Brisbane” scoring system (a simplified RSV severity scoring system)

1. Elliot E et al. Lancet PIDJ 2004
3. Preziosi et al. CID 2003

2. Spokes et al NSW Public Health Bulletin, 2010



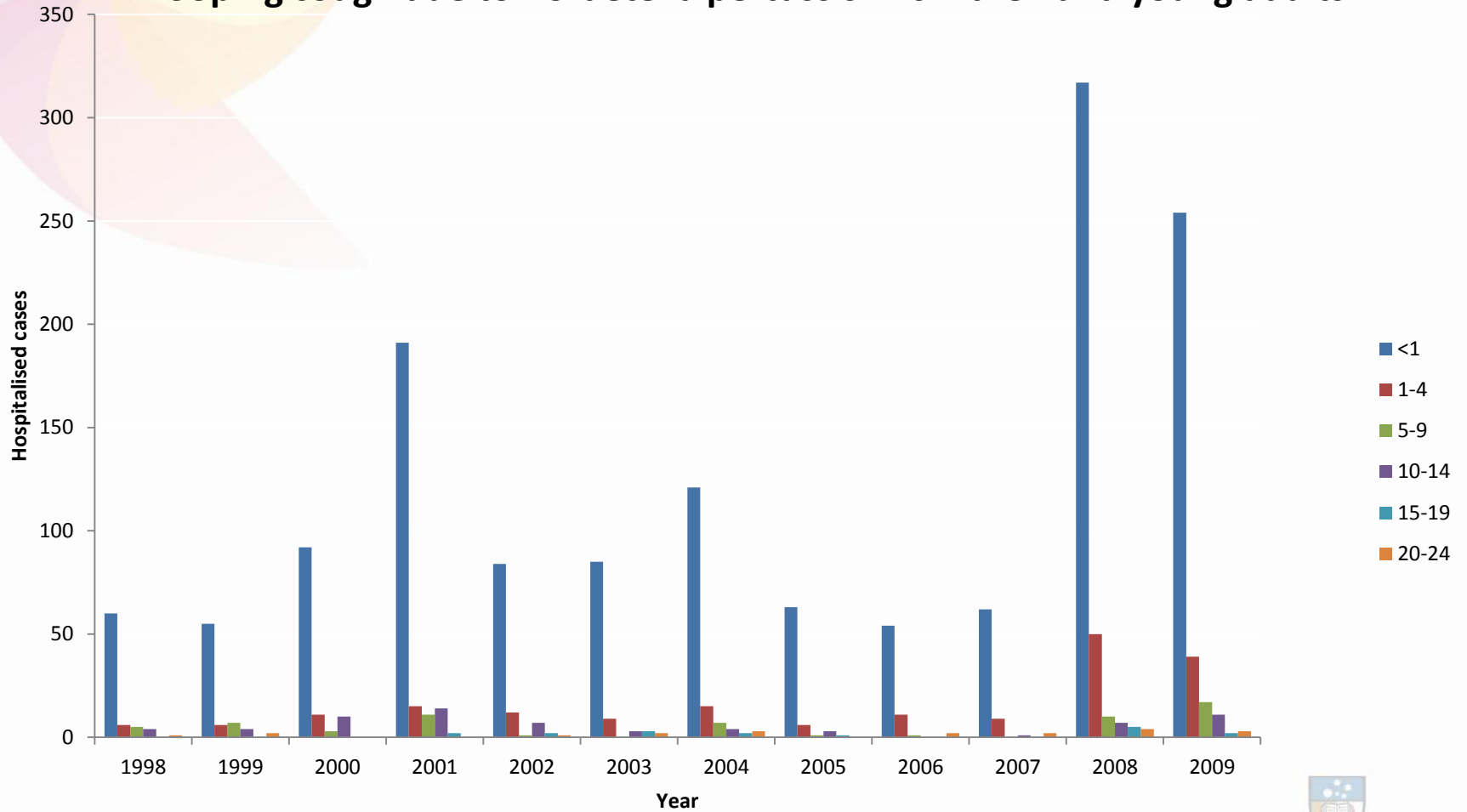
Separation statistics by principal diagnosis in ICD-10 Australia, 1998-2009



■ Whooping cough (Bordetella pertussis)

<http://www.aihw.gov.au/data-cube/?id=10737418525&libID=10737418524>

Whooping cough due to *Bordetella pertussis* in children and young adults



Study Aims

- To describe the clinical severity of pertussis infection in hospitalised children in Australia (all mainland states) during an epidemic period
- To determine risk factors associated with severe hospitalised pertussis cases in Australia
- To validate use of a pertussis severity scoring system to assess severity of disease in hospitalised cases
- To determine pertussis genotypes associated with severe disease



Study Design

- **cross-sectional**, prospective, **multicentre**, observational study to determine the clinical severity of pertussis infection and risk factors for severe disease in children admitted to hospital over a **12 month period** (01 May 2009 – 30 April 2010) during an epidemic.
- National, multicentre study
 - Adelaide (WCH and FMC)
 - Sydney (CHW)
 - Perth (PMH)
 - Melbourne (RCH)
 - Brisbane (RCH)
 - Canberra (CH)
 - Darwin (DH)



Study Methods

- Children (aged 0-17) admitted to hospital with a laboratory confirmed or clinical diagnosis of pertussis between 01 May 2009 and 30 April 2010.
- Questionnaire including demographic and clinical details + medical note review following consent
- Pertussis cases scored using a novel pertussis severity scoring system
- NPA samples available sent for genotyping (A/Prof Ruiting Lan, Uni NSW)
- Descriptive statistics, comparison of proportions by chi square testing, and multivariable analysis



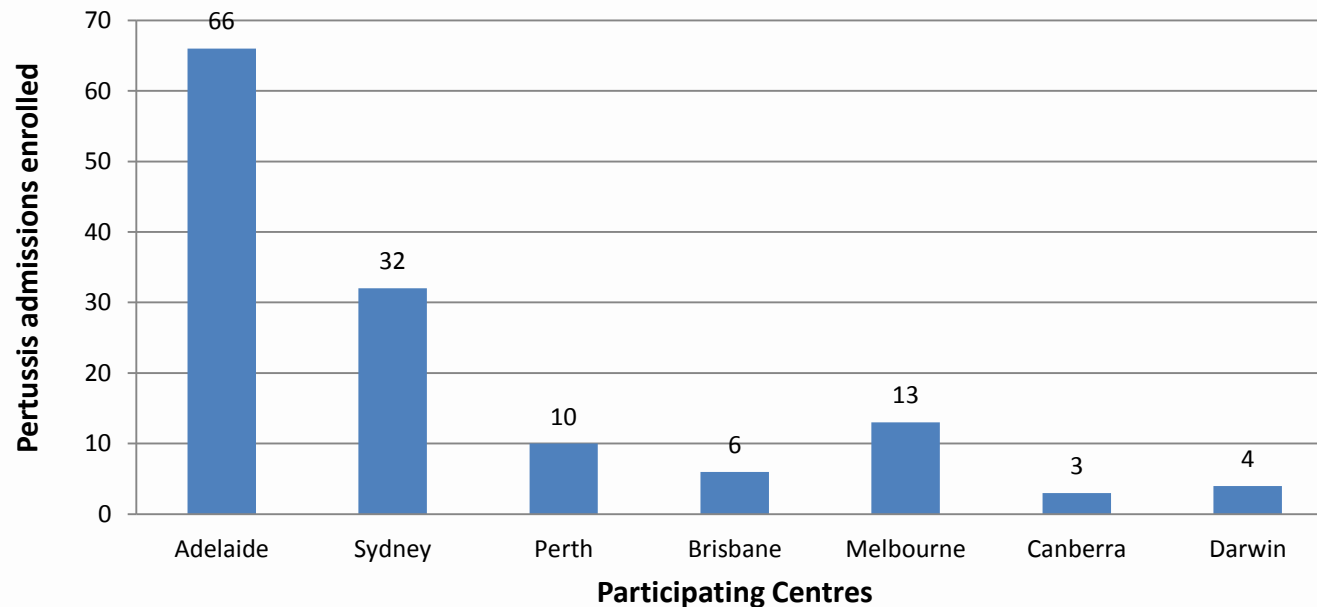
Pertussis severity scoring system

Pertussis severity score for children hospitalised with pertussis infection

	Grade 1	Grade 2	Grade 3
Apnoea Frequency	up to 1 per day	2-5 per day	>5 per day
Duration of hospitalisation	< 24 hours	1-7 days	> 1 week
Level of hospitalisation	General ward	HDU	ICU
Hydration Requirement	Nasogastric	IV hydration <48hrs	IV hydration >48hrs
Respiratory support	Suction/oxygen	CPAP	Ventilation
Presence of complications	Hypoxia Chest x-ray changes	Pneumonia	Encephalopathy Cardiomyopathy
TOTAL	6	12	18

Study population

140 children enrolled over 12 month period, 134 evaluable and met inclusion/exclusion criteria (43% of admissions < 20 yrs during this period)



* note – Adelaide included 2 hospitals (WCH, FMC)



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Results

Age

- Median: 2.4 months [IQR: 1.1 – 11.7 months]
- Mean: 18.2 months [Range: 10 days to 17 years of age]
- 67% were < 6 months of age
- 44.0% were < 2 months of age

Gender

- F:M 65:72 (47.4%, 52.6%)

Ethnicity

- Indigenous/Torres Strait Islander 9.0% (n=13)



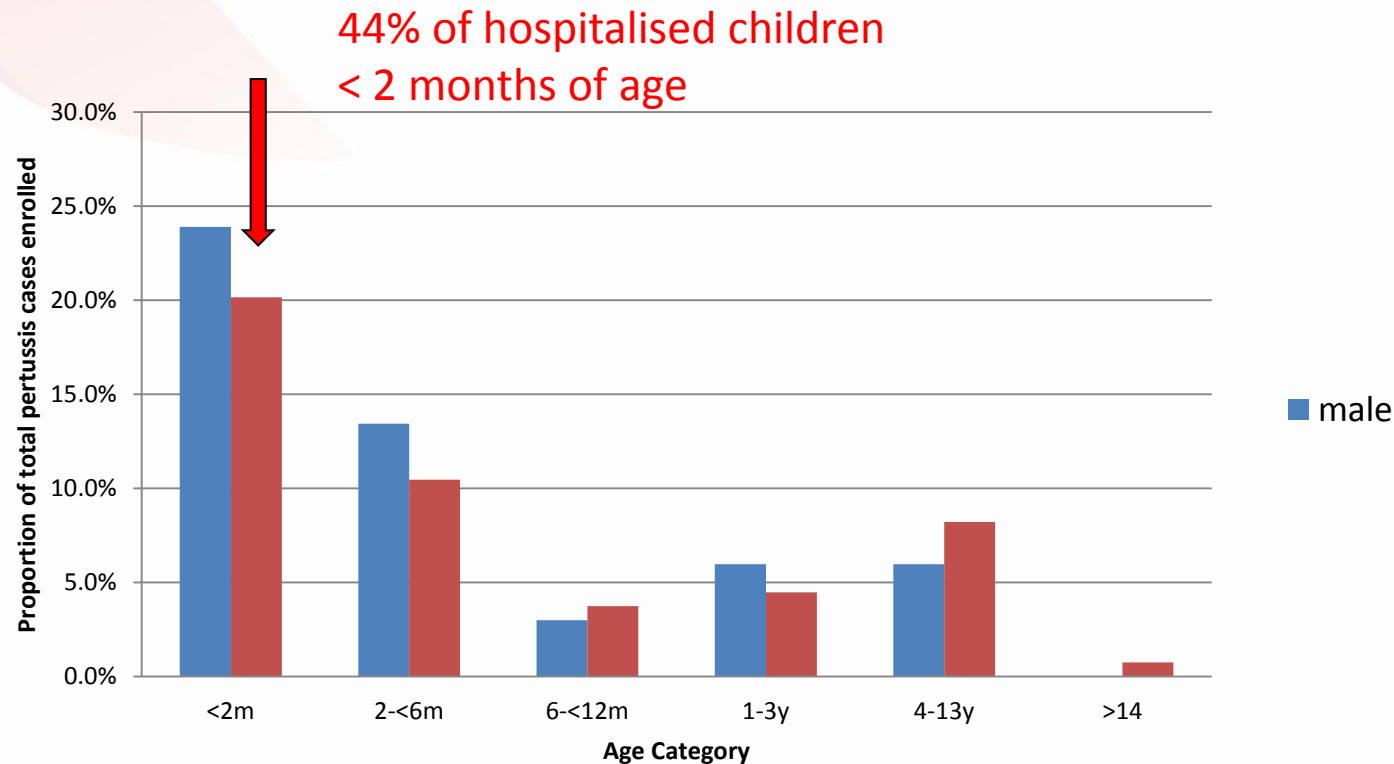
Pertussis diagnosis

Hospital	Total enrolled	PCR confirmed	Clinical diagnosis	% PCR confirmed
Women's and Children's Hospital, Adelaide	38	37	1	97.4%
Princess Margaret Hospital, Perth	10	8	2	80.0%
Royal Children's Hospital, Melbourne	13	6	7	46.2%
Flinders Medical Centre, Adelaide	28	27	1	96.4%
Royal Children's Hospital, Brisbane	6	6	0	100.0%
Royal Canberra Hospital, Canberra	3	3	0	100.0%
Darwin Hospital, Darwin	4	0	4	0.0%
Westmead Children's Hospital, Sydney	32	32	0	100.0%
TOTAL	134	119	15	88.8%



Severity of pertussis in Australia

Results



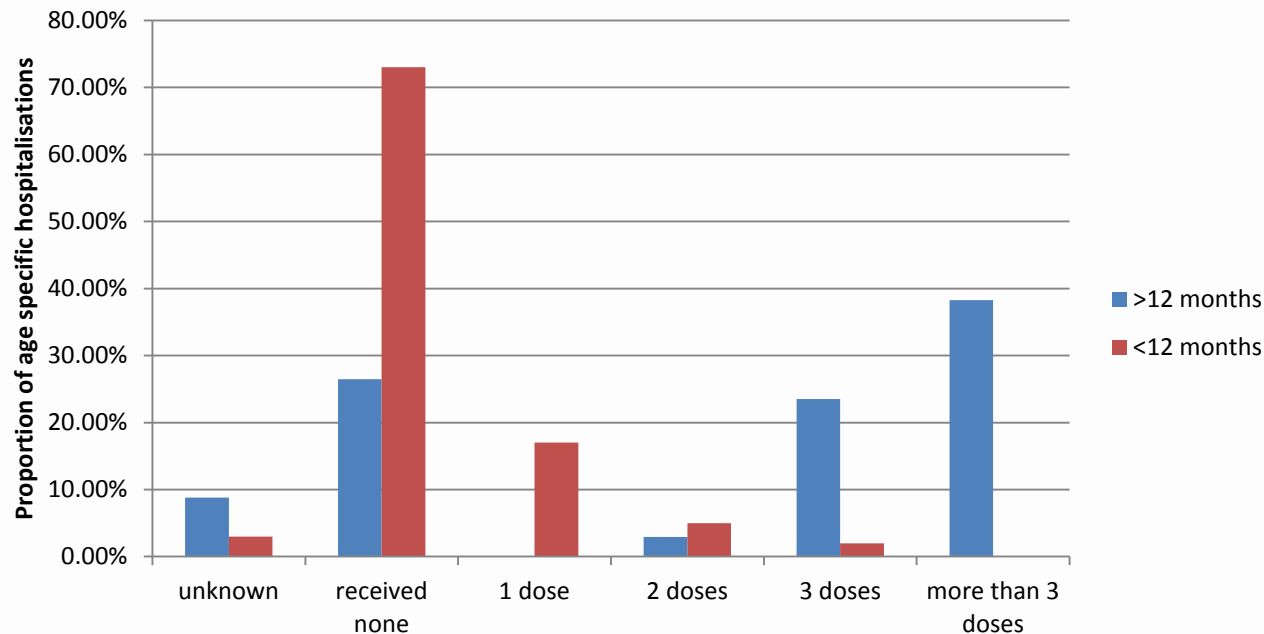
Age and Gender distribution for hospitalised pertussis cases enrolled in pertussis severity study in Australia (01 May 2009 -30 April 2010)



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Immunisation status

- 73/100 (73%) of children less than 12 months of age admitted for pertussis had received no pertussis containing vaccine
 - 30% were > 2 months of age
- 22/34 (65%) of children >12 months of age admitted for pertussis had received ≥ 3 pertussis containing vaccines



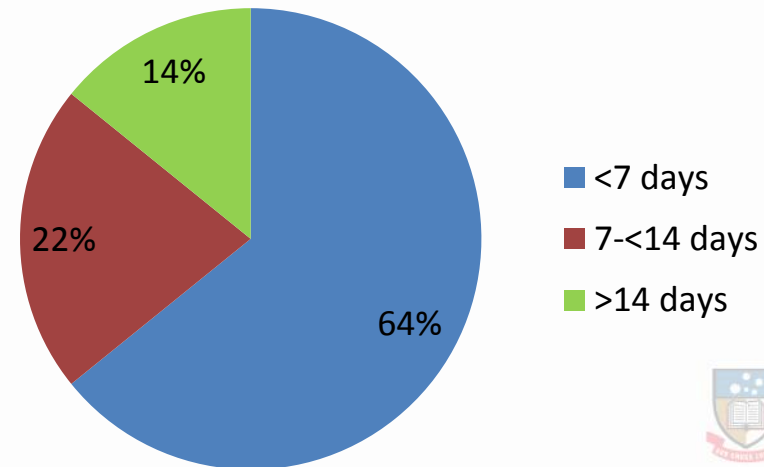
Duration of hospitalisation

Duration of hospitalisation (n=134)

Median duration = 4 days [IQR 2-10 days]

Range 1-48 days

- < 7 days = 86 (64.2%)
- 7-14 days = 29 (21.6%)
- >14 days = 19 (14.2%)



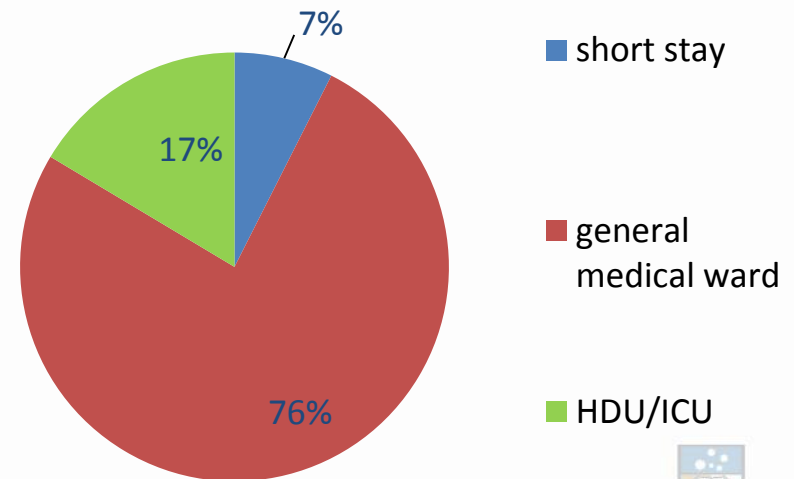
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Level of hospitalisation

Level of Hospitalisation (n=134)

- > Short Stay Ward = 10 (7.5%)
- > General Medical Ward = 102 (76.1%)
- > PICU = 22 (17%)



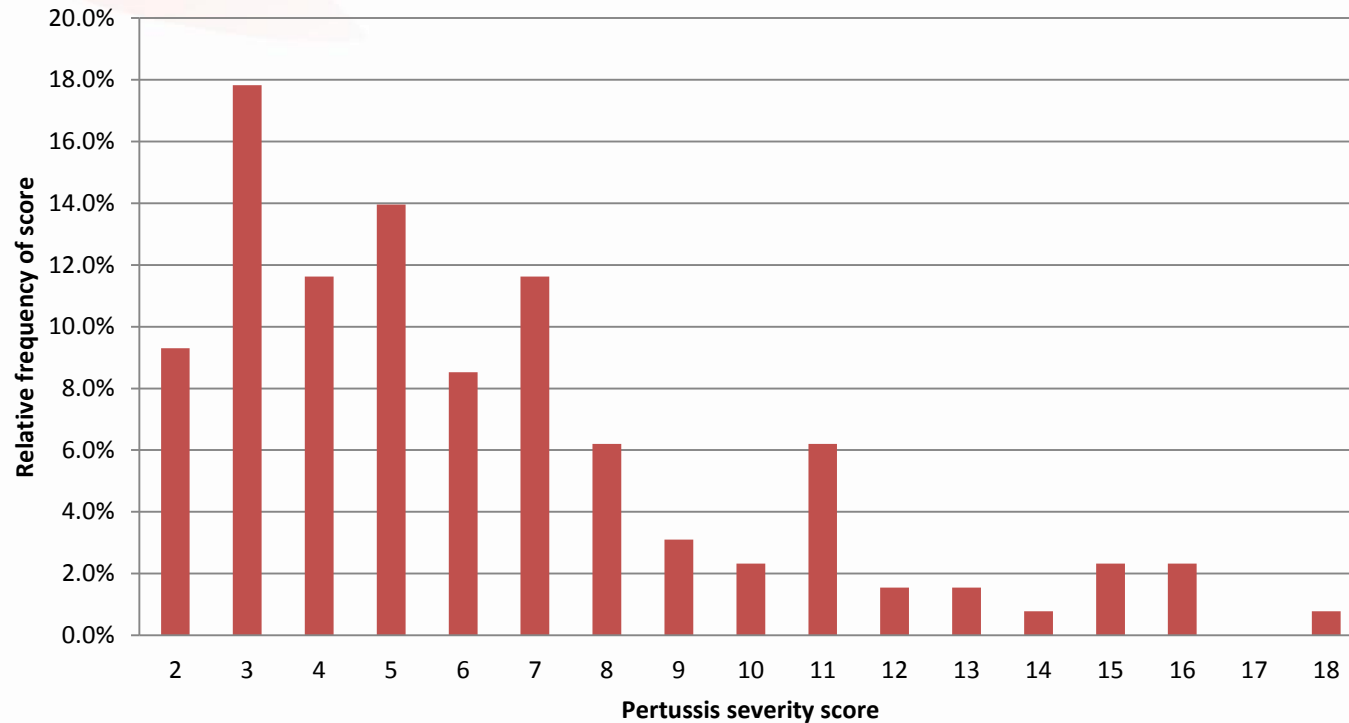
Clinical Features

Variable	< 1 year N=100		1-17 years N=34		Difference in proportions
	N	%	N	%	
Cough	92	92	33	97	P=0.31
Post-tussive Vomiting	76	58	18	52.9	P=0.61
Whoop	43	43	15	44.1	P=0.91
Coryza	40	40	14	41.2	P=0.90
Apnoea	40	40	3	8.8	P<0.001
Cyanosis	37	37	6	17.7	P=0.037
Fever	16	16	16	47	P<0.001
Wheeze	15	15	13	38.2	P=0.004
Bradycardia	14	14	0	0	P=0.021
Seizures	1	1	1	2.9	P=0.43
Respiratory Distress (any)	35	35	17	50	P=0.12

Pertussis Severity Score

- > 96% (129/134) received a pertussis severity score
- > 60% (79/137) received a score of ≤ 6 (graded as mild)

Distribution of pertussis severity score assigned to pertussis hospitalisations



Pertussis Severity Score by Age

Age	N	Median score	Score range (2-18)	Score ≥ 7 (severe) %
All	129	5	(2-18)	38.8%
<2m	56	7	(2-18)	55.5%
2-<6m	30	4	(2-11)	23.3%
6-<12m	9	6*	(2-16)	44.4%
12m-<4y	14	5.5	(3-15)	35.7%
>4y	20	3.5	(2-13)	15.0%

* Note – 3 of the 9 cases within this age category (6-<12m) had received no vaccinations

Children <2 months had highest median pertussis score
 Children >4 years had the lowest median pertussis score.



Pertussis severity score by Indigenous status

Gender	n	Median pertussis severity score	Range (2-18)	% ≥ 7 (severe)
All	129	5	(2-18)	38.8
Indigenous	12	6.5	3-14	46.2
Non Indigenous	105	5	2-18	36.2
Unknown	16	5	2-12	37.5



Predictors of severe disease

Parameter	Median PSS (IQR)	Proportion with PSS \geq 7	Chi square (proportions)	Relative risk (95%CI)
Age < 2 months	7	55.5%	P=0.001	2.2 (1.3, 3.8)
Presence of co-infection	7	53.1%	P=0.035	1.7 (1.1, 2.6)
Lymphocytosis \geq 20,000	11	84.6%	P=0.026	1.7 (1.2, 2.3)
Bradycardia	10	85.7%	P<0.001	2.6 (1.9, 3.6)

Clinical signs and symptoms on presentation to PED

Oxygen saturation <96%	8 (4-9)	56.0%	P=0.042	1.7 (1.1, 2.3)
Episodes of bradycardia	9 (6.5-11)	75.0%	P=0.030	2.1 (1.3, 3.3)
Post-tussive vomiting	6 (4-8)	47.2%	P=0.032	1.6 (1.0, 2.7)
Any respiratory distress	7 (5-9.3)	52.0%	P=0.012	1.7 (1.1, 2.6)

Co-infection

A total of 35 co-infective agents were identified

- 3 participants had two additional co-infective agents

Co-infective agent	Number of participants with co-infection
Rhinovirus	12
Respiratory Syncytial Virus	8
Adenovirus	3
Human Metapneumovirus	2
H1N1 influenza	2
Mycoplasma	2
Staph Aureus	2
Parainfluenza	1
Klebsiella	1
Oral candida	1
Streptococcus	1



Pertussis transmission data

Source of transmission

47% of cases had an identified confirmed or possible source of transmission

Source N=79/134	Confirmed N=45	Possible N=34	%
Sibling	19	14	41.8
parent	12 (8M, 2F, 2 both)	12 (6M, 4F, 2 both)	30.4
Other relative	7	4	13.9
Hospital/midwife	4 (3 midwives, 1 patient)		5.0
School	2	2	5.0
Friend of family	1	2	3.8



Study Limitations

- Accuracy of data: Results reliant on accurate clinical documentation at time of admission
- Validity of the scoring system in assessing severe hospitalised cases
- Generalisability: Data presented on approximately 40% of paediatric hospitalised pertussis cases in Australia during a 12 month period during the current epidemic



Conclusions

- Most paediatric pertussis hospitalisations occur in infants < 6 months of age
- The majority of children admitted to hospital < 12 months of age have not received any pertussis vaccine
- Co-infection, young age (<2 months), and post-tussive vomiting, low oxygen saturation, and bradycardia on presentation are risk factors for severe hospitalised cases
- Lymphocytosis > 20,000 is associated with severe disease

Early identification of hospitalised children at increased risk of severe morbidity or mortality from pertussis may result in reduced deaths from pertussis



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Thank you



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