MJA
The Medical Journal of Australia

Appendix

**This appendix was part of the submitted manuscript and has been peer reviewed.
It is posted as supplied by the authors.**

Appendix to: Yin JK, Jayasinghe SH, Charles PGP, et al. Determining the contribution of *Streptococcus pneumoniae* to community-acquired pneumonia in Australia. *Med J Aust* 2017; 207: 396-400. doi: 10.5694/mja16.01102.

Appendices

Appendix 1: Search strategy

Database searches were conducted by a medical librarian to locate publications on community-acquired pneumonia in Australia. Both international and Australian-specific databases were searched including OVID Medline (1946 to May Week 1 2016), OVID Embase (1974 to 2016 Week 19), SCOPUS (1823 – May 2016), Web of Science databases including Science Citation Index Expanded (1900-May 2016), Social Sciences Citation Index (1956-May 2016), Arts & Humanities Citation Index (1975-May 2016), Conference Proceedings Citation Index-Science (1990-May 2016) and Conference Proceedings Citation Index-Social Science & Humanities (1990-May 2016), Cochrane Library databases including Database of Systematic Reviews (Issue 5 of 12, May 2016), Central Register of Controlled Trials (Issue 4 of 12, April 2016), Database of Abstracts of Reviews of Effects (Issue 2 of 4, April 2015), NHS Economic Evaluation Database (Issue 2 of 4, April 2015) and Health Technology Assessments (Issue 2 of 4, April 2016), and the Informit Health collection, which covers both published and unpublished literature sources. The latter is an Australian developed and focussed suite of databases including AMI - Australasian Medical Index Archive (1968 - December 2009), APAIS-Health - Australian Public Affairs Information Service – Health (1978 – June 2016), ATSIhealth - Aboriginal and Torres Strait Islander Health Bibliography (1900 – June 2016), AUSPORT Australian Sport Database (1989 – June 2016), CINCH-Health - Health Issues in Criminal Justice (1968 – June 2016), DRUG Database (1974 – June 2016) and HIVA - HIV/AIDS Database (1980 – June 2016).

Relevant database thesaurus and free text terms representing community acquired pneumonia infections, including 'community-acquired infections', 'pneumonia bacterial', 'pneumococcal infections', streptococc*, pneumonia*, were combined with terms denoting Australia, including all individual State and territory names. Truncation was used where necessary to ensure all variant term endings were included.

To ensure maximal retrieval, the only limit applied where available was to 'humans'; no other limits such as language or publication date were used. The last search was completed on 07 June 2016. Full search strategy details are available upon request to authors.

We did not include a separate search of grey literature as it predominantly comprises national and jurisdictional reports, which describe routine surveillance data limited to invasive pneumococcal disease but do not include any data on aetiology of CAP. In addition, some electronic databases we mentioned above already included unpublished literature sources.

Appendix Table 1: summary of characteristics & results of Australian studies with data on the proportion of community-acquired pneumonia due to pneumococci, by vaccination policy era and by study period

Study	Study design	Study period	Location	N of all & tested participants	Age (yrs); % of Indigenous	Inclusion criteria	Exclusion criteria	Diagnostic method of pneumococcal CAP	% of pneumococcal CAP (95% CI*)	Outcome of pneumococcal CAP
Studies reporting on the proportions of CAP episodes due to pneumococci (sorted by study period)										
Lim 1989[19]	Prospective analysis of hospitalised patients (ED/ICU admission unspecified)	Apr 1987 to Mar 1988; 1 yr	SA (single hospital)	• All: 106 • Tested (any method): 106	Mean=60; Indigenous status not reported	Not hospitalised in preceding 2 weeks, within 48 h of admission	• Immunocompromised • PNE secondary to lung cancer, pulmonary infarction, cerebrovascular accident or complication of other aetiology	Confirmed Dx • Blood or pleural fluid culture Probable Dx • Sputum culture + microscopic examination • Pneumococcal antigen detected in sputum *p.s. urinary antigen test (UAT) was also performed – unconcentrated; thus not used in diagnosis*	Blood culture N: 8/103 = 7.8% (3.4–14.7%) Sputum culture **N**: 16/90 = 17.8% (10.5–27.3%) Any method N: 28/106= 26.4% (18.3–35.9%)	Not given
Thompson 1997[22]	Retrospective analysis of hospital records (ED/ICU admission unspecified)	Jun 1992 to Feb 1993; 1 yr	QLD (single hospital: Cairns)	• All: 177 • Tested (any method): 115	Not given 74.6% aged ≥10 yrs; 51% Indigenous	Consecutive admissions with 'CAP'	Not Australian residents N=4	Re-examination of clinical notes (clinical Dx plus X-ray)	Blood culture N: 9/115 = 7.8% (3.6–14.3%) Sputum culture N: 12/58 = 20.7% (11.2–33.4%)	Not given

Study	Study design	Study period	Location	N of all & tested participants	Age (yrs); % of Indigenous	Inclusion criteria	Exclusion criteria	Diagnostic method of pneumococcal CAP	% of pneumococcal CAP (95% CI*)	Outcome of pneumococcal CAP
Elliott 2005[16]	Prospective analysis of hospitalised patients (	Mar 1999 to Feb 2000; 1 yr	NT (Royal Darwin Hospital)	• All: 167 • Tested (any method): 132	Mean=47-49 (Range=13-90) 48% Indigenous	≥13 yrs, with Dx ≤24 h of admission, new pulmonary infiltrate on X-ray + clinical findings	Hospitalisation in previous 2 wks, PNE related to lung carcinoma/TB, or on review due to alternate aetiology	Blood culture, sputum, or pleural fluid	<u>Blood culture</u> N: 9/132 = 6.8% (3.2–12.5%) <u>Sputum culture</u> N: 6/9 = 6.1% (2.3–12.9%)	Not given
Weatherall 2008[24]	Prospective analysis of ED patients	May to Nov 2004	NSW (Concord Hospital)	• All: 59 • Tested (any method): 59	Median=79 yrs (aged ≥14 yrs) ; Indigenous status not reported	Aged ≥14 yrs; Dx of PNE; a radiological infiltrate	Neutropenia; discharge from hospital in the preceding 7 days	• Culture of blood and/or sputum, or • UAT	<u>Blood culture</u> N: 0/41 = 0% (0–8.6%) <u>UAT</u> N: 9/59 = 15.3% (7.2–27.0%) <u>Sputum culture</u> N: 3/19 = 15.8% (3.4–39.6)	Not given
Charles 2008[15]	Prospective, multi-centred, analysis of ED patients	Jun 2004 to Sept 2006	Victoria (4), QLD (1) & WA (1) All but one	• All: 885 (1.1% Indigenous) • Tested (any method):	65.1 yrs (range: 18-100); 1%	Aged ≥18 yrs; chest radiograph ≤24 h after	Hospitalisation in the past 14 days; substantially immunosuppressed, parenteral	<u>Confirmed Dx</u> • Blood culture, or • UAT, or • PCR of nose & throat swabs, or	<u>Blood culture</u> N: 33/868 = 3.8% (2.7–5.3%) <u>UAT</u>	<u>Mortality in ≥65 yrs</u> %: 11.3% (5.0–21.0%) N: 8/71

Study	Study design	Study period	Location	N of all & tested participants	Age (yrs); % of Indigenous	Inclusion criteria	Exclusion criteria	Diagnostic method of pneumococcal CAP	% of pneumococcal CAP (95% CI*)	Outcome of pneumococcal CAP
			hospital tertiary referral	885	Indigenous	admission demonstrated acute PNE; ≥2 symptoms consistent with PNE within 48 h of admission	antibiotics prior to blood samples for culture, aspiration pneumonitis, active treatment withdrawn within 12 h because of a poor prognosis	• Purulent sputum cultured a predominant organism, compatible with Gram stain Presumed Dx • Purulent sputum cultured predominant organism, without compatible results from Gram stain • Serologic test suggestive of recent infection	N: 95/850= 11.2% (9.1–13.4%) Blood culture or UAT N: 103/875 =11.7% (9.7–14.1%) Sputum culture N: 40/524 = 7.6% (5.5–10.2%) Any method 123/885= 13.9% (11.7–16.4%)	ICU/HDU admission in ≥65 yrs %: 9.9% (4.1–19.3%) N: 7/71

Study	Study design	Study period	Location	N of all & tested participants	Age (yrs); % of Indigenous	Inclusion criteria	Exclusion criteria	Diagnostic method of pneumococcal CAP	% of pneumococcal CAP (95% CI*)	Outcome of pneumococcal CAP
Jeremiah 2013[18]	Retrospective analysis of hospitalised patients (14% from ICU/HDU)	Oct 2007 to Sept 2008 POST 23VPPV AND PCV	Victoria (Ballarat Hospital)	• All: 184 • Tested (any method): 137	Median=72 (IQR= 54–80) Mean=67 (SD=18) ; Indigenous status not reported	Aged ≥18 yrs; discharge Dx of CAP, clinical syndrome compatible with CAP, consolidation on chest radiograph	Suspected aspiration pneumonia; hospital acquired pneumonia; immunocompromised; transfer from another healthcare facility	• Blood culture, or • UAT, or • Sputum culture & microscopy, or • Serologic test, or • PCR of nose & throat swabs	<u>Blood culture</u> N: 1/110 = 0.9% (0.02–5.0%) <u>UAT</u> N: 2/52 = 3.8% (0.5–13.2%) <u>Blood culture or UAT</u> N: 3/120 = 2.5% (0.5–7.1%) <u>Sputum culture</u> N: 8/71 = 11.3% (5.0–21.0%) <u>Any method</u> N: 10/137 = 7.3% (3.6–13.0%)	Not given

Study	Study design	Study period	Location	N of all & tested participants	Age (yrs); % of Indigenous	Inclusion criteria	Exclusion criteria	Diagnostic method of pneumococcal CAP	% of pneumococcal CAP (95% CI*)	Outcome of pneumococcal CAP
Remond 2010 (prospective and retrospective)[20]	Prospective analyses	Jul 2006 to Jun 2007	Central Australia (Alice Springs Hospital)	Blood culture • 129 • 120 Sputum culture • 129 • 105	Median=44 yrs (33-55 yrs) 85% Indigenous	Aged ≥18 yrs; systems & signs of acute lower respiratory tract infection & radiological evidence of PNE	Possible hospital-acquired PNE (diagnosis >48 h after admission or inpatients In the past 2 wks), or immunosuppressed	• Blood culture • Sputum microscopy & culture	Blood culture N: 5/120 = 4.2% (1.4–9.5%) Sputum culture N: 6/105 = 5.7% (2.1–12.0%)	Not given
	Retrospective analyses	Jul 2005 to Jun 2006	WA (6 hospital in Kimberley)	Blood culture • 164 • 93 Sputum culture • 164 • 87	Median=44 yrs (36-60 yrs) 78% Indigenous	As above	As above	As above	Blood culture N: 4/93 = 4.3% (1.2–12.6%) Sputum culture N: 19/87 = 21.8% (13.7–32.0%)	Not given
Other studies (sorted by study period)										
Fuller 1995[2] (conference abstract)[‡]	No details	Nov 1993 to Nov 1994; 1 yr	Vic (1 hospital in Melbourne)	• All: 229 Tested (any method): 229	No details	CAP defined using "standard criteria"	Not given	"Standard microbiological tests"	Unknown method %: 8.7% (5.4–13.2%) N: 20/229	Not given
Skull 2009[21]	Case-cohort study	Apr 2000 to Mar 2002	Vic (2 large teaching hospitals	• All: 1952 Tested (any method):	Mean=78.4 yrs (95% CI=78.0-78.7)	Aged ≥65 yrs; ICD-10-AM codes	Nosocomial pneumonia was excluded (diagnosis >48 h	• Blood culture, or • UAT, or • Sputum culture &	Any method %: 0.6% (0.03–1.1%) N: 11/1854	Not given

Study	Study design	Study period	Location	N of all & tested participants	Age (yrs); % of Indigenous	Inclusion criteria	Exclusion criteria	Diagnostic method of pneumococcal CAP	% of pneumococcal CAP (95% CI*)	Outcome of pneumococcal CAP
			in Melbourne)	1854		J10-J18 in any of the 14 diagnostic code positions	after admission)	microscopy, or • Cerebrospinal fluid tap PCR of nose & throat swabs		
Tramontana 2010[23]	Retrospective analysis of pathology records of CAP patients	May 2007 to Apr 2008	Vic (3 Melbourne hospitals: 1 tertiary centre & 2 suburban teaching hospitals)	• All: 341 Tested (any method): 251	Mean=71.1 yrs (SD=17.1 yrs)	Aged ≥18 yrs; ICD-10 coded; consolidation on chest radiograph performed within 48 h of admission	Hospitalisation in the past 14 days; immunocompromised; active TB; chest injuries	Same as Charles 2008[15]	Blood & sputum culture Data not given UAT %: 17.2% (11.5–24.4%) N: 25/145 Any method %: 13.1% (9.2–18.0%) N: 33/251	Not given
Wilson 2005[25]	Retrospective analysis of ICU records	Jan 2001 to Jul 2003	NSW (2 Newcastle hospitals: John Hunter & Mater Misericordiae Hospitals)	• All: 96 Tested (any method): 96	59.5 yrs (range:21-88 yrs)	Aged ≥18 yrs; Dx of PNE & radiology evidence of consolidation ≤24 h of presentation	Hospitalisation in the past 10 days, classification of PNE as hospital-acquired, or emergence of an alternative Dx during follow-up	Confirmed Dx • Isolates from blood or pleural fluid Probable Dx • Growth of single potential pathogen from culture of sputum, endotracheal aspirate or bronchoalveolar lavage fluid, presence of moderate to profuse polymorphs on Gram stain, predominant organism on Gram stain, specimen obtained within 24 h of	Any method %: 13.5% (7.4–22.0%) N: 13/96	Mortality %: 23.1% (5.0–53.8%) N: 3/13

Study	Study design	Study period	Location	N of all & tested participants	Age (yrs); % of Indigenous	Inclusion criteria	Exclusion criteria	Diagnostic method of pneumococcal CAP	% of pneumococcal CAP (95% CI*)	Outcome of pneumococcal CAP
								admission or at the time of intubation		

** The 95% confidence intervals were calculated using Binominal Exact test*

‡ This was a conference abstract[2] & was cited by Charles CID 2008 paper.[15] No further publication using the same dataset was identified.

Appendix Table 2: the ranges of point estimates (point estimate only if single study) of the proportion of testing CAP episodes for pathogen identification, by category of studies, type of analysis, and diagnostic test

Category of studies	Diagnostic test	Retrospective analyses		Prospective investigations	
		% testing CAP episodes for pathogen identification (95% CI)	Studies	% testing CAP episodes for pathogen identification (95% CI)	Studies
Studies with Predominantly non-Indigenous participants*	Any method	73.6–100.0%	[18,23,25]	100.0% (both studies)	[15,19]
	Blood culture and/or UAT	65.2%	[23]	98.9%	[15]
	Blood culture	54.6–59.8%	[18,24]	69.5–98.1%	[15,19,24]
	UAT	16.6–42.5%	[18,21,23]	96.0–100.0%	[15,24]
	Sputum culture	38.3–38.6%	[22,23]	32.2–84.9%	[15,19,24]
Studies with Predominantly Indigenous participants†	Any method	64.4%	[17]	-	-
	Blood culture	56.7–65.0%	[20,22]	79.0–93.0%	[16,20]
	Sputum culture	32.8–53.0%	[20,22]	58.7–81.4%	[16,20]

** ≥50% of participants was non-Indigenous*

† ≥50% of participants was Indigenous

Appendix Table 3: summary of disease outcome of CAP due to pneumococci in Charles 2008

Disease category	% of ICU/HDU admission	Case fatality rate
Bacteraemic	ICU/HDU: 15.8% (95% CI 3.4–39.6%; 3/19)	10.5% (95% CI 1.3–33.1%; 2/19)
Non-bacteraemic	ICU/HDU: 2.6% (95% CI 0.1–13.8%; 1/38)	7.9% (95% CI 1.7–21.0; 3/38)
p value	0.067	0.741