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Appendix

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Appendix to: McCullough AR, Pollack AJ, Plejdrup Hansen M, et al. Antibiotics for acute respiratory infections in general practice: comparison of prescribing rates with guideline recommendations. *Med J Aust* 2017; 207: 65-69. doi: 10.5694/mja16.01042.

Appendix: Antibiotic prescribing for acute respiratory infections in general practice: comparing current practice with guideline recommendations

SUPPORTING INFORMATION FILES

Table 1. List of ICPC-2 symptom/complaints codes not included in our analysis

R05	Cough
R07	Sneezing/nasal congestion
R08	Nose symptom/complaint, other
R09	Sinus symptom/complaint (incl pain)
R21	Throat symptom/complaint
R23	Voice symptom/complaint
H01	Pain, ear/earache
H04	Ear discharge

Table 2. Therapeutic Guidelines antibiotic prescribing recommendations for selected acute respiratory infections

Diagnosis (ICPC-2 code)	Therapeutic guidelines recommendations[1,2]
Acute rhinosinusitis (R74, R75)	• Avoid the routine use of antibiotic therapy. • Consider antibiotic therapy for patients for the following (symptoms of bacterial infection): ▪ Symptoms of rhinosinusitis > 7 days, with purulent nasal discharge, sinus tenderness (particularly unilateral) or maxillary toothache ▪ severe symptoms and high fever (39°C or higher) at the onset of illness and lasting > 3 days ▪ worsening symptoms after initial improvement ('double sickening').
Acute bronchitis Acute bronchiolitis (R78)	• Acute bronchitis commonly follows viral upper respiratory tract infection. Antibiotics are only rarely needed. • Acute bronchiolitis affects infants. Antibiotics are not indicated in the outpatient management of acute bronchiolitis.
Acute otitis media (H71)	• For most children, initial antibiotic therapy is not indicated. • Suppurative complications remain common in certain patient groups (e.g. some Aboriginal and Torres Strait Islander communities) and antibiotic therapy is usually indicated for patients in these communities. • *Children with systemic features:* • Initial antibiotic therapy is recommended for all children with systemic features (high fever, vomiting or lethargy) and may be required in children younger than 6 months without systemic features. • *Children without systemic features:* ▪ In children <6 months, symptomatic treatment alone may be appropriate initially; however, if antibiotic therapy is not used initially, review the child after 24 hours. If bilateral AOM or AOM with discharge is present, treat as for a child with systemic features (see above). ▪ In children >6 months or older, symptomatic treatment is recommended. If symptoms persist >2 days, or worsen, review the patient and consider starting antibiotic therapy. When review will be difficult, an alternative strategy is to provide a 'wait-and-see-prescription', where a prescription for antibiotic therapy is provided at the initial assessment and the patient or carer is advised to start therapy if the child fails to improve within 2 to 3 days, or if symptoms worsen at any time.
Acute pharyngitis and/or tonsillitis (R72, R76)	• Avoid the routine use of antibiotic therapy. • Antibiotic treatment is recommended for those who are: ▪ 2 to 25 years old from Indigenous communities in central and northern Australia, Maori and Pacific Islander people. ▪ Any age with existing rheumatic heart disease ▪ Have scarlet fever • Outside these high-risk patient groups, nonsuppurative complications of S. pyogenes infection are now so rare in Australia that routine antibiotic use is no longer indicated. • It is reasonable to prescribe antibiotic therapy for unwell patients and/or patients with particularly severe clinical features suggestive of streptococcal infection…high fever, tender cervical lymphadenopathy, tonsillar exudate and the absence of cough have some discriminatory capacity…the likelihood of streptococcal infection is higher when the majority or all of these clinical features are present, particularly in combination with other features suggestive of systemic illness.
Community acquired pneumonia (R81)	• Adults: antibiotic treatment of community acquired pneumonia is usually empirical. • Children: After the neonatal period, up to 70% of CAP in children is viral. Acute viral bronchiolitis is the most likely diagnosis in an infant younger than 18 months who presents with cough and respiratory distress. Oral antibiotic therapy is preferred in mild CAP; children with severe pneumonia usually require IV therapy initially. Infants and children with pre-existing cardiac or pulmonary disease require prompt and intensive treatment for CAP.
Pertussis (R71)	Antibiotic treatment is recommended to prevent disease transmission.
Laryngitis (R77)	No recommendations for Laryngitis.
Influenza (R80)	Antibiotic therapy is not indicated unless the clinical presentation suggests bacterial pneumonia, or if a secondary bacterial pneumonia develops.

Notes: we assume

- the recommendation for laryngitis approximates to zero use. This is supported by a Cochrane review, Reveiz L, Cardona AF. Antibiotics for acute laryngitis in adults. Cochrane Database Syst Rev. 2015(5):CD004783, which concludes "Antibiotics do not appear to be effective in treating acute laryngitis when assessing objective outcomes..."
- the recommendation for influenza also approximates to zero use (unless complicated by secondary bacterial pneumonia, in which case the recommendation for *Community Acquired pneumonia* applies).

Table 3. PubMed search strategy (up to July 2015)

Diagnosis	PubMed search strategy
Acute rhinosinusitis	((((("Morbidity"[Mesh] OR "Epidemiology"[Mesh] OR Morbidity OR Morbidities OR Prevalence OR Prevalences OR Incidence OR Incidences OR Epidemiology OR Epidemiological)) AND ("Australia"[Mesh] OR Australia[Tiab] OR Australian[Tiab] OR Australasian[Tiab] OR Australasia[Tiab] OR Queensland[Tiab] OR Victoria[Tiab] OR "New South Wales"[Tiab] OR Tasmania[Tiab]))) AND ("Rhinitis"[Mesh] OR "Sinusitis"[Mesh] OR Rhinitis OR Sinusitis OR rhinosinusitis OR (Nasal AND (Inflammation OR Inflamed OR Infection OR Infections OR Infected)))
Acute otitis media	((((("Morbidity"[Mesh] OR "Epidemiology"[Mesh] OR Morbidity OR Morbidities OR Prevalence OR Prevalences OR Incidence OR Incidences OR Epidemiology OR Epidemiological)) AND ("Australia"[Mesh] OR Australia[Tiab] OR Australian[Tiab] OR Australasian[Tiab] OR Australasia[Tiab] OR Queensland[Tiab] OR Victoria[Tiab] OR "New South Wales"[Tiab] OR Tasmania[Tiab]))) AND ("Otitis Media"[Mesh] OR "Otitis Media" OR ("Middle Ear" AND (Inflammation OR Inflamed OR Infection OR Infections OR Infected)))
Acute pharyngitis and/or tonsillitis	((((("Morbidity"[Mesh] OR "Epidemiology"[Mesh] OR Morbidity OR Morbidities OR Prevalence OR Prevalences OR Incidence OR Incidences OR Epidemiology OR Epidemiological)) AND ("Australia"[Mesh] OR Australia[Tiab] OR Australian[Tiab] OR Australasian[Tiab] OR Australasia[Tiab] OR Queensland[Tiab] OR Victoria[Tiab] OR "New South Wales"[Tiab] OR Tasmania[Tiab]))) AND ("Pharyngitis"[Mesh] OR Pharyngitis OR Pharyngitides OR Sore Throat OR Sore Throats OR Tonsillitis OR (Throat AND (Inflammation OR Inflamed OR Infection OR Infections OR Infected)) OR (Tonsils AND (Inflammation OR Inflamed OR Infection OR Infections OR Infected)))

Table 4. Prevalence of bacterial sinusitis in patients with acute rhinosinusitis

Study outcome	n with outcome	Total participants	Prevalence (%)	Reference
Have bacterial sinusitis				
Complication of common respiratory disease: sinusitis	53	11134	0.5	5
Antral aspiration – purulent secretions identified	2	100	2	6
We excluded those with high fever (38.5) and an overall clinical impression that antibiotic treatment was absolutely required	-	-	4	7
Not improved - still had fever with or without increasing signs and symptoms of respiratory tract infection at the end of the 7th day. Complicated - developed additional respiratory tract symptoms or signs of infection of other systems with suggestive evidence of bacterial etiology.	4	87	5	8
1 of 3 presentations compatible with a diagnosis of acute bacterial sinusitis (ABS): children with persistent symptoms, children with acutely worsening symptoms, and children with severe symptoms	139	2135	7	9
Clinical sinusitis (no definition)	10	142	7	10
Sinusitis complicating upper respiratory infection was considered when children had persistent upper respiratory infection symptoms for >10 days without improvement or an abrupt increase in severity of symptoms, fever, or purulent nasal discharge before day 10 of illness	Not reported	Not reported	8	11

Table 5. Prevalence of rheumatic heart disease, scarlet fever and severe symptoms in patients with acute pharyngitis and/or tonsillitis

Study outcome	Prevalence per 1000	Prevalence of RHD in indigenous or non-indigenous population (%)	Prevalence in total Australian population (%)[a]	Reference
Have rheumatic heart disease (RHD)[b]				
Indigenous Australians				
Prevalence of RHD in high risk (indigenous)	8 per 1000 children	0.86	0.03	12
Prevalence in Far North Queensland and Kimberley	Not reported	1.07	0.03	13
RHD in indigenous Australians in the Top End	12 per 1000	1.18	0.04	14
All age prevalence of RHD in indigenous Australians in the Northern Territory	19 per 1000	1.9	0.06	15
All age prevalence of RHD in indigenous Australians in the Northern Territory	>25 per 1000	2.5	0.08	16
Maximum rate of RHD in indigenous Australians	Not reported	5	0.15	17
Non-indigenous Australians				
Prevalence of rheumatic heart disease in low risk (non-indigenous) children	0 per 1000 children	0	0	12
Prevalence of rheumatic heart disease in non-indigenous Australians	0.4 per 1000	0	0	14
All age prevalence of RHD in non-indigenous Australians in the Northern Territory	0.26 per 1000	0.03	0.03	16
Scarlet fever	**New cases in Australia**	**New cases of acute pharyngitis in Australia, per year[d]**	**Prevalence in total Australian population (%)**	**Reference**
Scarlet fever notifications Winter 2013-2014[c]	1378	773000	0.18	18
All four of: high fever, tender cervical lymphadenopathy, tonsillar exudate and the absence of cough	**n with outcome**	**Total participants**	**Prevalence (%)**	**Reference**
3 or 4 “positive findings”: presence of tonsillar exudate, swollen anterior cervical nodes, presence of cough, history of fever	69	405	17	19
“3 or 4 predictors present”: fever history, swollen tender anterior cervical nodes, tonsillar exudates, lack of cough	-	-	30	20
“Centor score of 3 or 4”: fever >38°C, tender lymphadenitis, tonsillar coating, absence of cough	-	-	39	21

[a]We multiplied the prevalence in indigenous populations by the proportion of the Australian population that are indigenous (3%[3]) to get a prevalence in indigenous people as a proportion of the total Australian population. We multiplied the prevalence in non-indigenous Australians by the proportion of the Australian population that are non-indigenous (97%) to get the prevalence in non-indigenous Australians as a proportion of the total Australian population.

[b]Australian data

[c]3752 cases of scarlet fever in the UK, based on a UK population of 64600000, that is an incidence rate of 5.81 per 100000. We were unable to identify data that estimated the incidence of scarlet fever in Australia. The UK data were the only data we could identify for a developed nation. The UK rates were estimated during a spike in scarlet fever incidence and may be an overestimation of the Australian incidence rates. We have assumed this is likely to be the highest incidence rate that could exist in the Australian population (23714300[4]).

[d]BEACH data extrapolated to the annual number of cases of acute pharyngitis

Table 6. Prevalence of systemic features and symptoms that persist or worsen at day 2 in patients with acute otitis media

Study outcome	n with outcome	Total participants	Prevalence (%)	Reference
Systemic features (high fever, vomiting or lethargy)				
Acute otitis media severity of symptoms scale (severe symptoms, score 12-14)	34	291	12	22
Severe disease categorized by "previously published scoring criteria"	68	512	13	23
Symptoms (that persist or worsen) at day 2				
Absence of improvement or increasing symptoms after at least 3 days of treatment	4	84	5	24
No improvement in overall condition by day 3 (self-report from parental diary)	22	158	14	25

REFERENCES

1. *Therapeutic Guidelines: Antibiotic*. Melbourne, Australia: Therapeutic Guidelines Limited; 2014.
2. *Therapeutic Guidelines: Respiratory, Version 5*. Melbourne, Australia: Therapeutic Guidelines Limited; 2014.
3. Australian Bureau of Statistics. Experimental estimates and projections, Aboriginal and Torres Strait Islander Australians. http://www.abs.gov.au/ausstats/abs@.nsf/0/946D4BC28DB92E1BCA25762A001CBF38?opendocument.
4. Australian Bureau of Statistics. Population clock. http://www.abs.gov.au/ausstats/abs@.nsf/Web+Pages/Population+Clock?opendocument.
5. Dingle JH, Badger GF, Jordan Jr WS. Illness in the Home. A Study of 25,000 Illnesses in a Group of Cleveland Families: The Press of Western Reserve University; 1964.
6. Berg O, Carenfelt C, Rystedt G, Anggård A. Occurrence of asymptomatic sinusitis in common cold and other acute ENT-infections. Rhinology. 1986;24(3):223.
7. Kaiser L, Morabia A, Stalder H, Ricchetti A, Auckenthaler R, Terrier F, et al. Role of nasopharyngeal culture in antibiotic prescription for patients with common cold or acute sinusitis. European Journal of Clinical Microbiology & Infectious Diseases. 2001;20(7):445-51.
8. Lexomboon U, Duangmani C, Kusalasai V, Sunakorn P, Olson LC, Noyes HE. Evaluation of orally administered antibiotics for treatment of upper respiratory infections in Thai children. J Pediatr. 1971;78(5):772-8.
9. Wald ER, Nash D, Eickhoff J. Effectiveness of amoxicillin/clavulanate potassium in the treatment of acute bacterial sinusitis in children. Pediatrics. 2009;124:9-15.
10. Kaiser L, Lew D, Hirschel B, Aukenthaler R, Morabia A, Heald A, et al. Effect of antibiotic treatment in a subset of common cold patients who have bacteria in nasopharyngeal secretions. Lancet. 1996;347:1507-10.
11. Revai K, Dobbs LA, Nair S, Patel JA, Grady JJ, Chonmaitree T. Incidence of acute otitis media and sinusitis complicating upper respiratory tract infection: the effect of age. Pediatrics. 2007;119:e1408-12.
12. Roberts K, Maguire G, Brown A, Atkinson D, Remenyi B, Wheaton G, et al. Echocardiographic screening for rheumatic heart disease in high and low risk Australian children. Circulation. 2014;129(19):1953-61.
13. Remond MG, Severin KL, Hodder Y, Martin J, Nelson C, Atkinson D, et al. Variability in disease burden and management of rheumatic fever and rheumatic heart disease in two regions of tropical Australia. Intern Med J. 2013;43(4):386-93.
14. Carapetis JR, Currie BJ, Mathews JD. Cumulative incidence of rheumatic fever in an endemic region: a guide to the susceptibility of the population? Epidemiol Infect. 2000;124(2):239-44.
15. Parnaby MG, Carapetis JR. Rheumatic fever in indigenous Australian children. J Paediatr Child Health. 2010;46(9):527-33.
16. McDonald M, Towers R, Andrews R, Benger N, Fagan P, Currie B, et al. The dynamic nature of group A streptococcal epidemiology in tropical communities with high rates of rheumatic heart disease. Epidemiol Infect. 2008;136(04):529-39.
17. White H, Walsh W, Brown A, Riddell T, Tonkin A, Jeremy R, et al. Rheumatic heart disease in indigenous populations. Heart, Lung and Circulation. 2010;19(5):273-81.
18. Guy R, Williams C, Irvine N, Reynolds A, Coelho J, Saliba V, et al. Increase in scarlet fever notifications in the United Kingdom, 2013/2014. Euro Surveill. 2014;19:20749.
19. Wigton RS, Connor JL, Centor RM. Transportability of a decision rule for the diagnosis of streptococcal pharyngitis. Arch Intern Med. 1986;146(1):81-3.
20. Centor RM, Witherspooon JM, Dalton HP, Brody CE, K L. The diagnosis of strep throat in adults in the emergency room. Med Decis Making. 1981;1:239-46.
21. Hedin K, Bieber L, Lindh M, Sundqvist M. The aetiology of pharyngotonsillitis in adolescents and adults - Fusobacterium necrophorum is commonly found. Clin Microbiol Infect. 2015;21:263.e1-7.

22. Hoberman A, Paradise JL, Rockette HE, Shaikh N, Wald ER, Kearney DH, et al. Treatment of acute otitis media in children under 2 years of age. New England Journal of Medicine 2011;364:105-15.
23. Le Saux N, Gaboury I, Baird M, Klassen TP, MacCormick J, Blanchard C, et al. A randomized, double-blind, placebo-controlled noninferiority trial of amoxicillin for clinically diagnosed acute otitis media in children 6 months to 5 years of age. CMAJ. 2005;172:335-41.
24. Neumark T, Molstad S, Rosen C, Persson LG, Torngren A, Brudin L, et al. Evaluation of phenoxymethylpenicillin treatment of acute otitis media in children aged 2-16. Scand J Prim Health Care. 2007;25:166-71.
25. Tahtinen PA, Laine MK, Huovinen P, Jalava J, Ruuskanen O, Ruohola A. A placebo-controlled trial of antimicrobial treatment for acute otitis media. N Engl J Med. 2011;364:116-26.