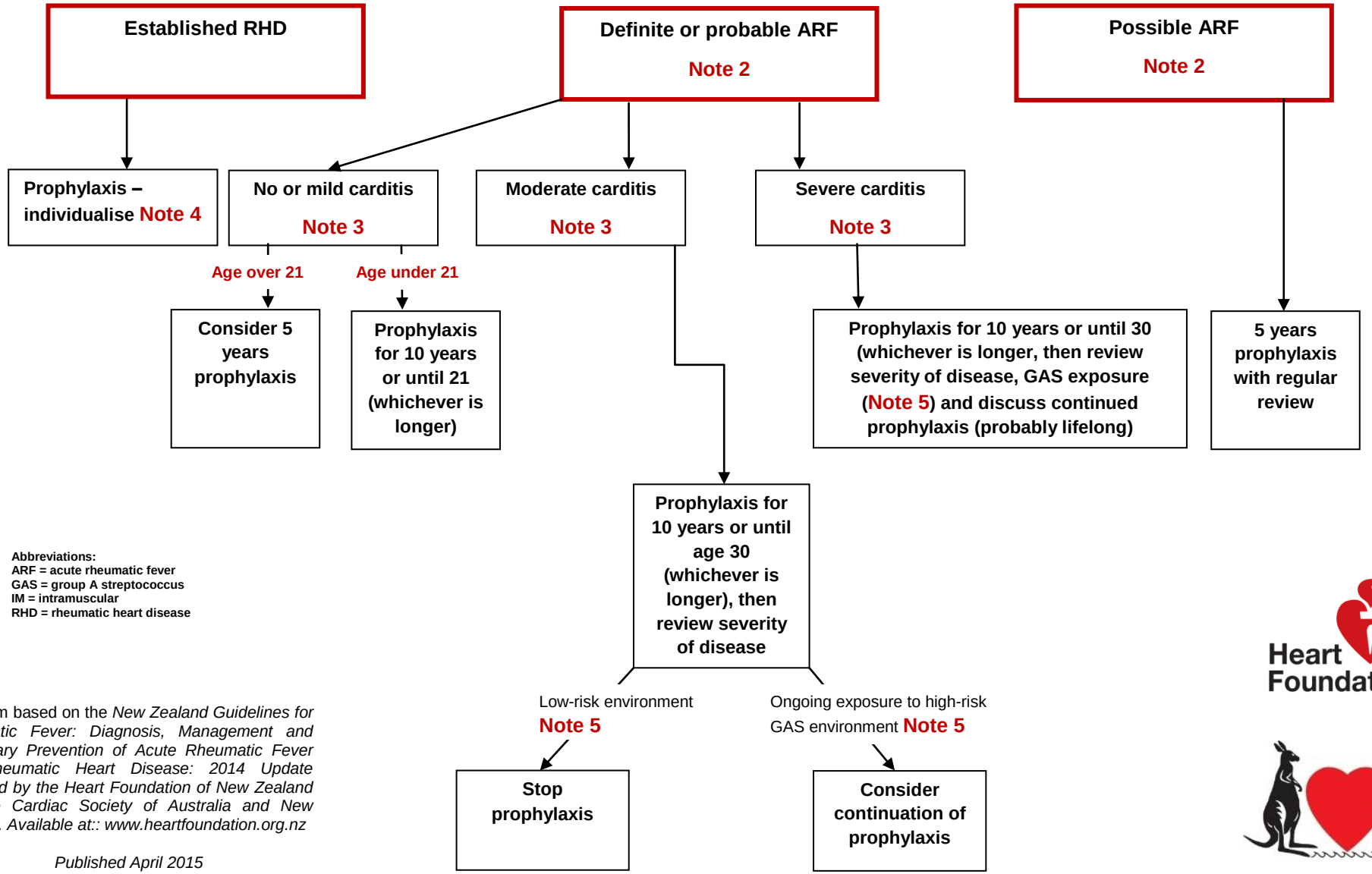
Algorithm 3: Guide for the duration of secondary prophylaxis in acute rheumatic fever (ARF)

New Zealand standard recommendations are for 4-weekly (28-day) IM BPG prophylaxis. A 21-day prophylaxis schedule is recommended only for those who have had confirmed recurrent ARF despite full adherence to 4-weekly prophylaxis. **Note 1**



Abbreviations:
ARF = acute rheumatic fever
GAS = group A streptococcus
IM = intramuscular
RHD = rheumatic heart disease

Algorithm based on the *New Zealand Guidelines for Rheumatic Fever: Diagnosis, Management and Secondary Prevention of Acute Rheumatic Fever and Rheumatic Heart Disease: 2014 Update produced by the Heart Foundation of New Zealand and the Cardiac Society of Australia and New Zealand. Available at:: www.heartfoundation.org.nz*

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Note 1

Antibiotic Regimens for Secondary Prevention of Acute Rheumatic Fever/Rheumatic Heart Disease

Antibiotic	Dose	Route	Frequency
First line			
Benzathine penicillin*	**Children <30kg**: 450mg (600,000 U) **Children & Adults ≥30kg:** 900mg (1,200,000 U)	Most effectively given as a deep intramuscular injection[1]	4-weekly (28 days), or 3-weekly for those who have had confirmed recurrent ARF despite full adherence to 4-weekly benzathine penicillin†
Second line (If intramuscular route is not possible or refused)‡			
Penicillin V	**Children <20kg:** 250mg	Oral	Two or three times daily
	Adolescents & Adults ≥20kg: 500mg	Oral	Two or three times daily
Following documented penicillin allergy§			
Erythromycin ethyl succinate (EES)	**Children & Adults:** 40mg/kg per day	Oral	2-3 divided doses (max adult daily dose 1000mg)

* *Benzathine penicillin can be given with lignocaine to reduce injection site pain*

† *The timing of administration may be advanced to aid compliance for extenuating circumstances such as tangi leave, overseas travel, school holidays etc. For people on a 28 day regimen it can be advanced as much as 14 days, and for those on a 21 days regime, up to 7 days.*

‡ *Oral penicillin is less efficacious than benzathine penicillin in preventing GAS infections and subsequent recurrences of ARF.[1,2,3,4] Twice-daily oral regimens are also likely to result in poorer rates of adherence over long periods of time[5] and less predictable serum penicillin concentrations, when compared to intramuscular benzathine penicillin.[6] In addition, oral penicillin V incurs a cost to the patient, while IM benzathine penicillin is free when provided through an ARF prevention programme. Oral penicillin should be reserved for cases who refuse intramuscular benzathine penicillin (Level II, Grade B - see Guideline Update). If a patient is offered oral penicillin, the consequences of missed doses must be emphasised and adherence carefully monitored (Grade D)*

§ *The benefits of long-term benzathine penicillin administration outweigh the rare risk of serious allergic reactions to penicillin and fatality as a result of anaphylaxis.[6,7,8,9] The rates of allergic and anaphylactic reactions to 4 weekly benzathine penicillin are 3.2% and 0.2%, respectively, and fatal reactions are exceptionally rare.[9,10] There is no increased risk with prolonged benzathine penicillin use. A prospective study of 1,790 ARF/RHD patients found similar rates of allergic reactions in those receiving long-term penicillin therapy and those receiving short-term therapy for sexually transmitted diseases (Level III-2).[10] Before commencing penicillin treatment, cases should be carefully questioned about known allergies to penicillin and other beta-lactam antibiotics. When patients state they are allergic to penicillin or when a non-specific reaction has been reported but there is no unequivocal evidence, they should be investigated for penicillin allergy, preferably in consultation with an immunologist/allergist. The options include skin testing[10] or a supervised challenge test. Most of these patients are not truly allergic. Penicillin desensitisation is not applicable to these patients, even with a regimen of more frequent injections, as it would have to be repeated before each dose of benzathine penicillin.[11,12] A RAST (RadioAllergoSorbent Test) may be used as a screening tool only. Because this is a specific but not very sensitive test, a negative RAST test must be followed up in all cases with penicillin skin testing and/or consideration of a graded challenge if appropriate (Grade D).*

Note 2

New Zealand Guidelines for the Diagnosis of Acute Rheumatic Fever

	Diagnostic Requirements	Category
Initial episode of ARF	2 major **or** 1 major **and** 2 minor manifestations **Plus** evidence of a preceding GAS infection*	Definite ARF
Initial episode of ARF	1 major and 2 minor with the inclusion of evidence of a preceding GAS infection* as a minor manifestation (Jones, 1956)[13]	Probable ARF
Initial episode of ARF	Strong clinical suspicion of ARF, but insufficient signs and symptoms to fulfil diagnosis of definite or probable ARF	Possible ARF
Recurrent attack of ARF in a case with known past ARF or RHD	2 major **or** 1 major and 2 minor **or** several† minor **plus** evidence of a preceding GAS infection* (Jones, 1992)[14]	Recurrent ARF
Major manifestations: modified‡ from Jones 1992 (see Table 5 in Guideline Update for key points in identifying major manifestations)	Carditis (including evidence of subclinical rheumatic valve disease on echocardiogram)§ Polyarthritis‖ **or** aseptic monoarthritis (with or without a history of NSAID use)* Chorea (can be stand-alone for ARF diagnosis) Erythema marginatum Subcutaneous nodules	
Minor manifestations: (see Table 5 in Guideline Update for key points in identifying minor manifestations)	Fever Raised ESR or CRP Polyarthralgia‖ Prolonged P-R interval on ECG	

Categories of Definite, Probable and Possible ARF can be determined by the application of the New Zealand criteria to each case (see Table 4 and 5 in the Guideline Update).

All categories assume that other more likely diagnoses have been excluded. Please see additional tables for details about specific manifestations.

CRP=C-reactive protein; ECG=electrocardiogram; ESR=erythrocyte sedimentation rate; GAS=group A streptococcus; RHD=rheumatic heart disease

* *Elevated or rising antistreptolysin O or other streptococcal antibody (Table 6 in the Guideline Update), is sufficient for a diagnosis of definite ARF. A positive throat culture or rapid antigen test for GAS alone is less secure as 50% of those with a positive throat culture will be carriers only. Therefore, a positive culture alone demotes a case to probable or possible ARF.*

† *Most cases of recurrence fulfil the New Zealand criteria. However in some cases (such as new carditis on previous RHD) it may not be clear. Therefore in order to avoid under-diagnosis, a presumptive diagnosis of rheumatic recurrence may be made where there are several minor manifestations and evidence of a preceding GAS infection in a person with a reliable history of previous ARF or established RHD. In addition, WHO (2004) recommendations state that where there is established RHD, a recurrent attack can be diagnosed by the presence of two minor manifestations plus evidence of a preceding group A streptococcal infection.*[15]

‡ *Acceptance of echocardiographic evidence of carditis as a major criterion was the New Zealand modification to the Jones (1992) update*

§ *When carditis is present as a major manifestation (clinical and/or echocardiographic), a prolonged P-R interval cannot be considered an additional minor manifestation in the same person*

‖ *Other causes of arthritis/arthralgia should be carefully excluded, particularly in the case of monoarthritis e.g. septic arthritis (including disseminated gonococcal infection), infective or reactive arthritis and auto-immune arthropathy (e.g. juvenile chronic arthritis, inflammatory bowel disease, systemic lupus erythematosus, or other systemic vasculitis and sarcoidosis. Note that if polyarthritis or monoarthritis is present as a major manifestation, polyarthralgia cannot be considered an additional minor manifestation in the same person.*

Special consideration should be given to high-risk population groups such as Māori and Pacific people, and those residing in poor socio-economic circumstances. In these cases, it may be important to err on the side of diagnosis and prophylaxis.

Note 3

Severity of Acute Rheumatic Fever Carditis

Mild Carditis*
• Mild mitral or aortic regurgitation clinically and/or on echocardiography (fulfilling the minimal echocardiographic standards in Table 8 in the Guideline Update) without heart failure, without cardiac chamber enlargement on CXR, ECG or echocardiography
Moderate Carditis

• Any valve lesion of moderate severity on clinical examination **or**
• Cardiac chamber enlargement seen on echocardiogram **or**
• Any valve lesion graded as moderate on echocardiogram†
  ◦ Regurgitation is considered moderate if there is a broad high-intensity proximal jet filling half the left atrium i.e. Mitral or a lesser volume high-intensity jet producing prominent blunting of pulmonary venous inflow[16]
  ◦ Aortic regurgitation is considered moderate if the diameter of the regurgitant jet is 15% to 30% of the diameter of the left ventricular outflow tract with flow reversal in upper descending aorta[16]

Severe Carditis

• Any impending or previous cardiac surgery for RHD, **or**
• Any valve lesion associated with significant cardiomegaly or heart failure, **or** graded as severe on clinical examination
• Any valve lesion graded as severe on echocardiogram:
  ◦ An abnormal regurgitant colour and Doppler flow patterns in pulmonary veins is a prerequisite for severe mitral regurgitation in children[16]
  ◦ Doppler reversal in lower descending aorta is required for the diagnosis of severe aortic regurgitation in children.[16]
  ◦ In adults, Doppler flow reversal in the pulmonary veins (for severe MR) or abdominal aorta (for severe AR) is specific if present, but can be more difficult to detect; their absence does not exclude severe regurgitation if not detected.

* *Valvular regurgitation is usually relatively mild in the absence of pre-existing disease; in first episodes of ARF, severe mitral and aortic regurgitation occurred in less than 10% of patients in New Zealand*[16]

† *When there is both mitral and aortic regurgitation, one must be moderate by echo criteria in order for the carditis to be classified of moderate severity.*

Tricuspid and pulmonary regurgitation graded mild or greater may be seen in people with normal hearts who have fever, volume overload or pulmonary hypertension. **For this reason a diagnosis of carditis should not be based on right-side regurgitation alone.** Although pulmonary and tricuspid regurgitation are often seen in association with left-sided lesions in ARF, pressure and volume overload must be excluded before attributing even moderate tricuspid regurgitation to valvulitis. If both left and right-sided lesions coexist in ARF carditis, then the predominant influence for diagnosis is the severity of the left-sided lesion.

Note 4

For those presenting with RHD for whom no initial episode of ARF can be identified, the decision to commence penicillin prophylaxis should be taken on an individual basis with regard to the age of the patient, severity of the disease, possible age of first attack and risk of exposure to GAS. See also page 46 in the Guideline Update.

It is recommended that cases with established valvular disease have regular dental care and follow the guidelines for endocarditis prophylaxis.

Note 5

Individuals working or living with children, or in a living situation where there is overcrowding or close proximity to others (such as boarding schools, barracks and hostels), have a higher risk of exposure to GAS and subsequent development of ARF. In these cases, consideration should be given to extending the duration of prophylaxis.

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