Secondary prophylaxis with penicillin for rheumatic fever or established rheumatic heart disease

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Date: January 7, 2021
Updated: April 22,2021

Description of condition and intervention

This intervention, long-term antibiotic prophylaxis for individuals with a history of rheumatic fever, aims to limit recurrence of rheumatic fever and progression to rheumatic heart disease (RHD). Acute rheumatic fever is an autoimmune disease that may occur two to three weeks following group A streptococcus (GAS) pharyngitis. Symptoms can include arthritis, carditis, involuntary movements of the arms and legs, trunk, and facial muscles, subcutaneous nodules, and erythema marginatum. Carditis due to rheumatic fever can lead to permanent damage of heart valves and this is referred to as chronic RHD. Acute treatment of rheumatic fever consists of anti-inflammatory therapy (aspirin or NSAIDs), oral antibiotic therapy (Penicillin/Amoxicillin 500 mg twice daily for 10 days), and heart failure management for those with severe carditis. No treatment has been shown to completely alter the progression of acute rheumatic fever to chronic rheumatic heart disease. However, secondary prophylaxis with penicillin can limit progression of established rheumatic valvular disease to more severe illness by preventing recurrent GAS infections. The recommended treatment is long-acting intramuscular penicillin G benzathine 1.2 to 2.4 million units as a single dose every 21 to 28 days for 5 to 10 years (Rheumatic fever without carditis: 5 years or until 21 years of age (whichever is longer), Rheumatic fever with carditis and residual heart disease: 10 years or until 40 years of age (whichever is longer), Rheumatic fever with carditis but no residual heart disease 10 years or until 21 years of age (whichever is longer)). Sources: BMJ Best Practice and UpToDate.

International guidelines

Organization	Duration of treatment for rheumatic fever or rheumatic heart disease
American Heart Association (2009)	Rheumatic fever (RF) with carditis and residual heart disease (persistent valvular disease based on clinical or echocardiographic findings): 10 years since last RF or until 40 years of age (whichever is longer)
	Rheumatic fever with carditis but no residual heart disease (no valvular disease*): 10 years or until 21 years of age
	Rheumatic fever without carditis: 5 years or until 21 years of age

Source: Gerber et al 2009

Intervention attributes

Type of interventions

Preventive

Delivery Platform of intervention

Primary care outpatient setting (Health centre and hospital) *(Watkins et al 2017)*

Equity

In addition to considerations like cost-effectiveness and health systems factors, dimensions of equity can be relevant for priority setting. The opportunity for a long and healthy life varies according to the severity of a health condition that individuals might have, so there are inequities in individuals' opportunities for long and healthy lives based on the health conditions they face. Metrics used to estimate the severity of illness at an individual level can be used to help prioritize those with less opportunity for lifetime health. FairChoices: DCP Analytics Tool uses Health adjusted age of death (HAAD), which is a metric that estimates the number of years lived from birth to death, discounting years lived with disability. A high HAAD thus represents a disease less severe in terms of lifetime health loss, while a low HAAD represents a disease that is severe on average, causing early death or a long period of severe disability. It is also possible to estimate the distribution of HAAD across individuals with a health condition. FairChoices shows for each intervention an average HAAD value of the conditions that are affected by respective interventions that have health effects. Additionally, a plot shows HAAD values for around 290 conditions (Johansson KA et al 2020).

Time dependence

Moderate level of urgency and treatment outcomes will not be highly affected by some days of delay.

Population in need of intervention

Children, adolescents, and young adults (age 5-39 years) with rheumatic fever and/or rheumatic heart disease are the treated population, and it may reduce the incidence rate of rheumatic heart disease of children, adolescents, and adults (<40years).

Intervention effect and safety

Prophylactic penicillin probably reduces rheumatic fever recurrences and streptococcal throat infections among children and adolescents with rheumatic fever or rheumatic heart disease (moderate certainty of evidence). The effect of prophylactic penicillin on mortality and adverse events among children and adolescents with rheumatic fever or rheumatic heart disease is uncertain (very low certainty of evidence). No studies reported the effects on rheumatic heart disease progression and disability among children and adolescents with rheumatic fever or rheumatic heart disease. Table 2 below summarises the effectiveness and safety of penicillin secondary prophylaxis. Source: *Fønhus et al 2020*

Table 1: Effect and safety of prophylactic penicillin on children and adolescents with rheumatic fever or rheumatic heart disease (From rapid review by Fønhus et al 2020)

What happens?	No prophylactic penicillin	Prophylactic penicillin	Certainty of evidence1
Rheumatic fever recurrences Prophylactic penicillin probably reduces rheumatic fever recurrences among children and adolescents with rheumatic fever or rheumatic heart disease (follow up: range 6 months to 5 years)	83 per 1 000 children	25 per 1 000 children (10 to 60) *	⊕⊕⊕◯ MODERATE
Streptococcal throat infections Prophylactic penicillin probably reduces streptococcal throat infections among children and adolescents with rheumatic fever or rheumatic heart disease (follow up: range 6 months to 2 years)	126 per 1 000 children	29 per 1 000 children (11 to 79) *	⊕⊕⊕◯ MODERATE
Rheumatic heart disease progression Not reported in the included studies (1 ongoing study will report on this)	Not reported in the included studies		
Mortality – all cause The evidence is very uncertain about the effect of prophylactic penicillin on all-cause mortality among children and adolescents with rheumatic fever or rheumatic heart disease (follow up: range 1 years to 5 years)	We do not report numbers of results of very low certainty		⊕◯◯◯ VERY LOW
Mortality – due to heart failure or carditis The evidence is very uncertain about the effect of prophylactic penicillin on mortality due to heart failure or carditis among children and adolescents with rheumatic fever or rheumatic heart disease (follow up: range 1 years to 5 years)	We do not report numbers of results of very low certainty		⊕◯◯◯ VERY LOW

Adverse events The evidence is very uncertain about the effect of prophylactic penicillin on adverse events among children and adolescents with rheumatic fever or rheumatic heart disease (follow up: range 6 months to 5 years)	We do not report numbers of results of very low certainty	⊕◯◯◯ VERY LOW
Disability/Quality of Life Not reported in the included studies	Not reported in the included studies	

Model Assumptions

Summary of model parameters and values used in FairChoices – DCP Analytical Tool

Category	Model parameter	Notes
Intervention	Long term prophylactic penicillin	
Cost calculation		
Treated population Prevalence of RHD		
Gender	Both male & female	
Age	5 to 19 years	
Treated fraction	1.25	
Effect calculation		
Affected population		
Affected gender	Both male & female	
Affected fraction age	5 to 39 years	
Affected fraction	1.25	Those with condition
Comparison	Other care	
Incidence reduction (RRR*) Rheumatic fever recurrence	0.7	Fonhus 2020

*Assumed for relative risk reduction (RRR), see below

Intervention cost

The cost per case treated per year is estimated to be USD 53.06, 2019, Kenya (Coates M et al 2021). Population in need (PIN) is estimated based on cases of RHD in ages 5-39 adjusted by a "treated fraction" of ~1.25.

References

BMJ Best Practice (https://bestpractice.bmj.com/topics/en-gb/404 accessed 15 Dec 2020)

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