Acute Rheumatic Fever in Indigenous children and young adults in Canada: a review of primary prevention strategies

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Abstract

Introduction: There is a growing disparity in the incidence of ARF between Indigenous and non-Indigenous people. ARF is common in school-aged children, particularly those who live in communities with overcrowded housing, poverty, and limited resources. In Manitoba, rates of ARF have greatly declined over the years; however, it continues to disproportionately affect First Nations (FN) people, especially in rural communities. There are currently no national or provincial ARF prevention strategies.

Objective: To evaluate primary prevention strategies and programs for ARF targeting Indigenous communities.

Methods: A literature review was conducted using the PubMed database for studies and trials. Keywords used were "streptococcal pharyngitis", "rheumatic fever", "rheumatic disease", "primary prevention". Articles that met the inclusion criteria were selected for review.

Results: Five articles were reviewed. All studies utilized school-based sore throat clinics for the detection and diagnosis of streptococcal pharyngitis and subsequent secondary prophylaxis with antibiotics. Four studies found a significant reduction in the incidence of ARF with the school-based intervention group to detect and diagnose streptococcal throat infections.

Conclusion: Data already exists showing the high incidence of ARF in FN people in Manitoba. School-based programs are effective in reducing the development of ARF. A coordinated effort is urgently needed to implement primary prevention programs in Manitoba.

Introduction

Background

Acute rheumatic fever (ARF) and its sequela, rheumatic heart disease (RHD) is a consequence of untreated or undertreated streptococcal pharyngitis, and it continues to be a global health problem (1). In 2013, there were 32.9 million people with RHD worldwide, with 275,000 deaths per year attributed to RHD (2).

ARF is an autoimmune response to Group A beta-hemolytic streptococcus (GAS) throat infections, and 60% of people with rheumatic fever will go on to develop RHD which causes carditis and valvular heart disease (3). ARF is diagnosed using the Revised Jones Criteria and may involve the heart, joints, and movement disorders (4). The global burden of disease of ARF is vast, as it can lead to the development of rheumatic heart disease and severe cardiac damage, causing significant morbidity and mortality in children and young adults in their greatest years of economic and social productivity. In developing nations, the national cost of ARF and RHD was estimated to be USD$50-$70 million annually per country, with each case of severe RHD costing nearly $50,000 in direct health costs (2, 3).

Rheumatic fever and Indigenous people

ARF is thought to be a disease from the past in developed countries, and the cases that do occur in these nations occur at disproportionately high rates among Indigenous children as seen in Native American and Indigenous Hawaiians in the United States, Indigenous, Fijians in Fiji, the Maori in New Zealand, and Aboriginals in Australia (5). The Aboriginals in the Northern Territory of Australia saw an annual ARF incidence of 250-350 per 100,000 children (6) and in New Zealand, the annual incidence of ARF of Maori and Pacific children was 10 times that of

children of European descent (5). These high rates are concentrated and persists in some of the poorest regions in the world (7).

In Canada, the incidence of ARF has largely declined, however it continues to disproportionately affect the First Nations (FN) population. In a retrospective study conducted by the Children's Hospital of Winnipeg and Variety Heart Centre, children diagnosed with ARF over 10 years (2000-2010) were identified. The study found that the overall annual incidence rate of ARF in the province of Manitoba was 4.748 per 100,000 for FN children and 0.618 per 100,000 for non-FN children (8). Madden and Kelly (9) study of First Nation children in North Western Ontario found an incidence of ARF at a rate of 8.33 cases per 100 000 persons. In 2015, the incidence of ARF in the First Nations people of Northwestern Ontario was 21.3 per 100,000, which was 75 times greater than the overall incidence in non-Indigenous Canadians (10). The disparity in rates among Indigenous people is likely to be multifactorial, including the host's genetic susceptibility to the streptococcal bacterium, and social and environmental factors that influence the spread of disease, such as low socioeconomic status, inadequate access to health care, and overcrowded households (5).

RHD is a global leading cause of cardiac death in children as they those that present with symptoms of the disease are in the late stages of rheumatic heart valve disease. ARF is a highly preventable disease once GAS pharyngitis is identified using the Jones Criteria. Secondary antibiotic prophylaxis with penicillin has been shown to prevent streptococcal infection from developing into rheumatic fever (5). Thus, early identification and improving the efficiency of detection and diagnosis are key in the prevention of ARF.

Nations like New Zealand have taken initiative showing the effectiveness of ARF and RHD primary and secondary prevention programs as outlined with the New Zealand Heart

Foundation (4) and World Heart Federation (11). Unlike these developed nations, there is currently no ARF prevention program in place in Manitoba and no national strategy aimed at ARF reduction. This study will focus on primary prevention strategies within Indigenous communities in developed nations given the disparity in the incidence of ARF in FN compared to non-FN in Canada.

Objective

In Canada, there are currently no studies or programs targeting the prevention of ARF and RHD in the Indigenous population. The purpose of this study is to review and identify types of primary prevention programs for ARF in Indigenous populations, specifically in the pediatric population. The objectives were to identify the methods of the programs, outcomes of the intervention, and identify any common themes in the programs. For this study, primary prevention refers to the diagnosis and treatment of GAS pharyngitis to reduce the development of rheumatic fever. This study will not be reviewing ARF primordial prevention, which are strategies that address the risk factors that would otherwise place an individual at risk of developing and spreading GAS pharyngitis.

Methods

A literature search was performed using the PubMed data in January 2020. Keywords included streptococcal pharyngitis, rheumatic fever, rheumatic disease, and primary prevention. Reference lists of articles relevant to the study objectives were also reviewed to identify additional articles. The New Zealand Heart Foundation (https://www.heartfoundation.org.nz/) and World Heart Foundation RHD statement document (11) was also reviewed. Titles and abstracts of all resulting articles were reviewed to eliminate studies irrelevant to the research questions and duplicates, using the inclusion and exclusion criteria outlined in Table 1.

As there is currently no national ARF reduction strategy in Canada, limited data and studies are to be expected. The main focus of this study is Manitoba, however, there is a lack of study on prevention programs to reduce the rates of ARF in Canada. The search found only one article that completed a study on ARF primary prevention in Canada (12). Thus, this review largely included studies completed outside of Canada. There are many nations besides Canada that have Indigenous communities with similar issues of higher rates of ARF than in the general population.

Results

Search Results

An initial search on PubMed resulted in 947 articles. After reviewing articles, three met the inclusion criteria. An additional 2 articles were added after reviewing the Heart Foundation of New Zealand and the World Heart Foundation. No recent studies were found; the studies reviewed were published between 1982-2009. One RCT study, one cross-sectional study, and three observational studies were reviewed. The 5 studies are summarized in Table 2. All studies utilized a form of school-based programs; four articles implemented school-based sore throat clinics (1,12-14) and one utilized school and community-based education (15) for the early detection and treatment of GAS pharyngitis. The schools were situated in Indigenous communities in New Zealand, Canada, and the United States. Although not an Indigenous community, one study held in Cuba was added for review as it targeted a high-risk region within the nation (15).

Description of Studies

The study by Lennon et al. (1) was the only RCT study reviewed and also the most recent study of the five articles. The study evaluated school-based control of ARF in the endemic region

of South Auckland, New Zealand in up to 22,000 children from 1998-2001. The study clearly outlined the design of the study and methods utilized; only schools with >70% of students of Indigenous Maori and Pacific Island children were invited to participate in the study (1). Consent was obtained from the parents, school board, and principal. Randomization methods of schools were clearly outlined. School-based intervention programs included a sore throat clinic with education, diagnosis, and secondary penicillin prophylaxis treatment to reduce the incidence of ARF. Classrooms were visited daily to ask if children had a sore throat and a trained worker would complete a throat swab which was couriered to a laboratory on the same day. Results were reported to the school nurse within 3 days. If GAS positive, a nurse would contact parents for verbal content to begin antibiotics. Secondary penicillin prophylaxis was delivered at school by nurses for 10 days. This ensured adherence to the medication regimen.

Chun et al. (13) showed the occurrence of ARF in ethnic groups of Hawaii following a 4-year school-based sore throat clinic. No information was provided for how schools were chosen and if any randomization occurred. The health aides in each school only obtained throat cultures of children (age 4-18) who reported to the school health teams with complaints of an upper respiratory tract infection. No information was provided on the training of these health aides. If cultures were positive for GAS, these children were referred to their medical providers for treatment. The study did not indicate how many of the students with sore throats were swabbed. An observational study utilized the Jones criteria to identify 36 cases of ARF in 63,484 school children with intervention, versus 29 cases of ARF 48,740 in schools with no sore throat program. Rates of ARF were 14.2 and 12.3 per 100,000 respectively; RR=0.68 (95% CI, 0.42-1.12) (13). The study collected demographic data on these children; their ethnic group and welfare status. Although they were able to demonstrate the high incidence of ARF in Samoan

children (incidence of 96.5 per 100,000 children compared to 9.0 per 100,000 in Causasian children), the study was not able to indicate whether rates of ARF declined in a particular ethnic group (13). The results only demonstrated that participating schools with sore throat clinics show a significant decline in rates of ARF than schools without the program. The study was able to indicate a link between socioeconomic status and occurence of streptococcal infections as rates of ARF were significantly higher in welfare children than non-welfare children in participating schools. Another limitation of this study was that it excluded children from the study if welfare status was unknown and if children were absent from school.

Coulehan et al. (14) completed an observational study of health records from 1975-1979 of a school-based sore throat clinic in Navajo Reservations in the United States (14). School participation was not randomly assigned. A visiting nurse to the schools on the Reservations reported inconsistent frequencies, as it depended on personnel and transportation". Throat swabs were taken from symptomatic and as well as asymptomatic children who may be potential carriers. A regimen of penicillin would be given if an individual was GAS positive. The study did not indicate the number of throat swabs completed, and whether children were repeatedly swabbed. The study found a significant decline in the rates of ARF in Navajo schoolchildren with school-based throat swabs. From a total of 29 cases of ARF, 7/29 cases of ARF attended schools with intervention, and 22/29 cases attended schools with no sore throat clinics (RR=0.39, 95% CI, 0.1-0.94) (14). There were inconsistent throat swabs in this study due to school children's absenteeism, and no follow-up was provided. The study indicated high costs of this program, due to swabbing and treating a vast number of asymptomatic children who tested positive for GAS. The study concluded that future program efforts should target symptomatic children with GAS pharyngitis and surveillance of asymptomatic children.

The article by Nicolle et al. (12) was the only Canadian study found. Community health workers would visit schools in Rankin Inlet, Nunavut and St. Theresa Point, Manitoba, to identify and culture Inuit and First Nation children with complaints of sore throats. (12). If swabs were positive for GAS pharyngitis, these children were treated with penicillin. This was not a good quality study as no time frame was given on when the study was completed, and the randomization method was unclear. The study did not report the number of schools visited, or the number of school children involved. There was also no mention of the rates of rheumatic fever and whether their intervention showed any clinically significant reduction of GAS pharyngitis in these two communities. Many children on an antibiotic regimen were also lost for follow-up. The study did indicate that all swab cultures were sent to Winnipeg, Manitoba for identification. This article highlights the need for further Canadian studies in the First Nations and Inuit population.

The study by Nordet et al. (15), carried out a ten-year prevention program from 1986-1996 in the Pinar del Rio province of Cuba (15). This region was chosen as it had one of the highest rates of ARF in Cuba with high severity of RHD requiring hospitalization and heart surgery. The study objective was to reduce the morbidity, disability and mortality of ARF and RHD by implementing community-based primary and secondary prevention strategies to prevent and control ARF and RHD. The study focused on reducing incidence and severity of ARF and RHD. This was done by increasing community awareness and health literacy which included additional training to health care workers, and education to the community including teachers, students, and parents, via pamphlets and media broadcast. Education was provided on the importance of early detection and treatment of GAS pharyngitis, follow-up for any possible ARF and RHD via echocardiography, and compliance with secondary antibiotic prophylaxis. Two

cross-sectional studies were completed on nearly 230,000- 280,000 school children aged (5-25 years old) at the beginning and end of the study using a multi-stratified random-sample method found a statistically significant decline in the incidence of ARF and RHD from 18.6 cases per 100,000 to 2.5 cases per 100,000 (15). The study also reported a significant decline in the severity of ARF and RHD which was measured by number of hospitalizations (heart failure, need for heart valve surgery), and echocardiogram showing ARF with no heart damage. Increased compliance with secondary prophylaxis was also reported however methods to collect this data was unclear. The study implemented several interventions at one time, thus it cannot be determined if one strategy was superior to the other. It was not explicitly indicated who was completing throat swabs and diagnosing sore throat, and no school-based sore throat clinics was mentioned. The study also did not indicate the socioeconomic status of the community and whether there were barriers to accessing a primary care provider. This was the only study that assessed the cost-effectiveness of the project, showing a significant decline (81%) in the direct cost of managing ARF and RHD. This decline can be due to lower number of individuals with severe disease, fewer hospitalizations, and nearly no cases of heart surgery in the later years (15). The results of this study show that prevention and control of ARF and RHD are feasible and cost-effective. A comprehensive approach to prevention should be taken, which involves the support of the community, school system, health system, and all levels of government.

Common Themes

Components and details of the prevention strategies were analyzed using the framework from the World Heart Foundation- *Tools for implementing rheumatic heart disease control programmes (TIPS) Handbook (11)*.

Burden of disease is evident

Before designing protocols and implementing prevention and control programs, a needs assessment must be completed to provide data to demonstrate population affected, the desired action and goal of policies, and the key stakeholders. Several studies provided information on the need for the programs, demonstrated by the evident high rates of ARF in their region. Although they did not clearly indicate whether a needs assessment was completed, they did briefly discuss the planning and organization that took place with stakeholders and funders such as community leaders, health providers, and government (1,15). The Coulehan et al. (14) study showed the complexities of how reservation schools and hospitals were funded, which may create barriers in communications, funding, and resource allocation. Recognition of the severity of this problem was key to the development of these school-based programs.

Collaboration amongst decision-makers

One study discussed the distrust of the Indigenous (Samoans) people towards Western Medicine and would approach traditional healers first (13). Only two studies briefly discussed the collaboration between the leaders of the Indigenous communities at the local and federal levels with health workers and researchers (1, 15). Involvement of the local community was necessary during the consultative process of program development and implementation. Respect and trust are key in every aspect of the process and are especially important in regard to cultural differences and practices. This collaboration and trust within the community were vital as approval was required from the school and parents to allow these studies to take place (1,13,14).

Program model and challenges

All studies utilized school-based or a form of community-based strategies that included sore throat clinics or education of teachers that reduced the incidence of new cases of ARF.

These school-based clinics were able to detect sore throats and ensure proper diagnosis of GAS pharyngitis. The social determinant of health this addresses is access to health care. As children are required to be in school by law in Canada and likely other nations, implementing health programs within schools would enable children to attend for health care especially in resource-limited communities.

School-based sore throat clinics relied on schoolchildren to attend school and to report sore throats to attend for care. Children absent from school were not included in the study (13-15) and follow-up must be completed to determine if they were symptomatic or not. Relying on symptomatic children to attend for care can be a barrier if a child withheld their symptoms from a teacher or school health worker. These programs relied on the accurate identification of a sore throat and diagnosis of GAS pharyngitis but only one study (15) indicated additional training and education of school teachers and health care staff. Thus, children with symptoms of GAS pharyngitis and ARF may be missed if personnel were not adequately trained.

Only one study discussed the location of laboratory testing for the throat swabs, which was in another city that was hours from the community (12). For studies with visiting health workers, there were inconsistent reporting on the frequency of school visits, as transportation and commutes into these communities appeared to be a barrier (14, 15).

Once diagnosed with GAS pharyngitis, prevention also relies on adequate treatment and adherence to the penicillin regimen to prevent the development of ARF and RHD. This literature review did not discuss compliance and adherence to antibiotic prophylaxis. The studies reviewed did not discuss how far the community was from the nearest health centre and did not comment on the accessibility of primary care physicians to initiate treatment of GAS pharyngitis. Only one study indicated that children with GAS positive sore throats were treated with antibiotics in

schools by a nurse (1), while other studies relied on family members to follow up with primary care providers for proper medication.

All studies failed to provide the demographics of the children studied including information on housing status, the number of people in the household, accessibility to health care and medicine, and household socioeconomic status. Data on social and environmental risk factors that would place them at risk of developing GAS pharyngitis and ARF would help identify potential areas to target in future prevention programs.

Sustainability

Empowering community members through education and enhancing community involvement may strengthen the longevity of these programs. To improve the sustainability of the programs, Lennon et. al. (1) discussed increasing the number of Maori and Pacific health providers in future program implementation, likely so communities were not dependent on visiting staff and to increase the trust and comfortability between children, families, and health providers. Another study indicated that a 'native community health worker' was used (12). None of the studies indicated the primary language of the community and health workers. Having Indigenous health workers may help alleviate cultural and language barriers. One study emphasized the importance of increasing community awareness and health literacy (15), especially in areas of low socioeconomic status and inadequate access to health care. These communities may be unaware of the connection between and the consequences associated with GAS pharyngitis, ARF, and RHD.

Only one study demonstrated the cost-effectiveness of the prevention and control of ARF and RHD (15) by promoting health literacy and awareness, subsequently reduced the severity of

disease. Some component of this study design can be adapted to other nations to target their population.

Discussion

Based on the results, school-based sore throat programs was most studied and has been shown effective in reducing the rates of ARF. These primary prevention strategies aimed to increase detection and treatment of GAS pharyngitis. The advantage of primary prevention over secondary prevention is the prevention of heart disease that would otherwise be seen in secondary antibiotic prophylactic treatment.

Statistics Canada census data from 2016 reported that First Nations people on reservations had the highest rate of overcrowding and were 4 times more likely to live in homes in need of major repairs (16). The 2010 Canada Auditor General Report stated that First Nations people on Reserve have significantly lower socioeconomic well-being than other Canadians using indicators in education, income, health (17). As ARF is linked to the social determinants of health, primordial prevention strategies should also be implemented as it focuses on minimizing the development of risk factors that contribute to acquiring and spreading GAS infections (18). In Canada, there appears to be a lack of strategy and guidelines specifically targeting the prevention of ARF. However, measures that aim to alleviate social disparities and overcrowding often seen Indigenous communities may reduce the incidence of ARF, as well as many other preventable infectious diseases often seen in these communities such as Tuberculosis (19). Closing this socioeconomic gap may help close the gap in health outcomes.

Although addressing issues of social inequalities is a complex issue, primary prevention strategies can improve health literacy and access to healthcare, which can significantly decrease

direct and indirect costs associated with ARF and its sequela. The costs of prevention programs in Canada remains to be evaluated; however, it is unlikely to exceed the long-term direct cost associated with ARF and RHD (15). Implementation of such programs are not without logistical barriers such as approval from communities, sources of funding, resource allocation, and coordination of key stakeholders. Another barrier would be overcoming the relationship between all levels of government, Health Canada, and the First Nations people given the history of Residential Schools, Missing and Murdered Indigenous Women, and systemic bias towards First Nations people. Nonetheless, efforts must be taken to develop a strategy in ARF prevention given the long term social and healthcare costs of the disease. As the health system serving First Nations on-reserve is multi-jurisdictional, federal, provincial and First Nations community health authorities must work together for communities to have effective services for GAS pharyngitis and ARF/RHD prevention, similar to what has been done for tuberculosis (19).

ARF and RHD is a public health issue with First Nations and Inuit people. However, the Public Health Agency of Canada (PHAC) currently does not monitor cases of rheumatic fever as it is not considered an invasive infection (20). From the PHAC websites, there is currently no childhood or adolescent programs or initiatives targeting GAS pharyngitis and rheumatic fever. A national initiative would help raise awareness and education to parents, educators and the communities on the consequences of GAS pharyngitis and relationship with ARF and RHD.

As there is no existing cure for ARF and RHD, the focus should be on prevention strategies. These strategies include reducing risk factors for streptococcal throat infections, and the detection, diagnosis, and treatment to reduce the risk of developing ARF and RHD. In Manitoba, there are physicians, physician assistants, and nurses who provide health care services to rural and remote areas of Manitoba and Nunavut that are largely First Nations and Inuit

Population. For these health care providers, understanding the social determinant of health and the social inequalities these communities face can improve health care delivery. There are currently no school-based sore throat clinics or trials in Manitoba. Thus clinicians must have a high index of suspicion for GAS pharyngitis and ARF in Indigenous children.

Limitations of Study

This literature review only used one search engine to find articles for reviews. Only one RCT study and one cross-sectional was found. Most of the studies reviewed were completed in the 1980s to 1990s, as there is limited data on primary prevention targeting Indigenous communities. No articles were found on new research on the efficacy of ARF prevention strategies in Indigenous communities. In Canada, no current research on ARF prevention has been completed since the study completed by Nicolle et al. (12).

Further epidemiological investigation in Canada is needed to determine the nature of the association between social determinants of health with ARF and RHD.

Conclusion

ARF and RHD have largely declined in Canada except for First Nations peoples highlighting a health disparity that requires further investigation and prevention measures. There is currently no national ARF reduction strategy in First Nation communities, despite evidence indicating high rates of ARF in First Nation children.

There is evidence that school-based primary prevention is effective in reducing the incidence of ARF in Indigenous communities; elements of these programs can potentially be integrated into Canada. ARF and RHD are lifelong issues with socioeconomic implications. Canada can learn from other developing nations who have implemented nation-wide strategies on rheumatic fever control and prevention.

ARF is a public health issue amongst First Nations people. This review strongly demonstrated the need for further research of primary prevention strategies in Canada. Further research and action include the development of needs assessments, development of program proposals, and pilot projects in First Nations communities. Action is urgently required.

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Appendix

Table 1: *Inclusion and exclusion criteria of literature search*

Inclusion criteria	***Exclusion criteria***
• Randomized controlled trials (RCTs), observational studies, ongoing trials, qualitative studies • Primary prevention of rheumatic fever • Articles written in English • Studies published after 1980 (inclusive) • Studies on ARF in Aboriginal, Indigenous, high-risk communities population groups • Focus on children and young adults	• Studies focusing on evaluating drug regimens • Sole focus on secondary prevention strategies • Studies on cost-benefit analysis • Literature reviews • Commentaries, forums, editorials

Table 2: **Overview of studies included for review**

Study	**Population**	**Type of study and Intervention**	**Details of program**	**ARF and RHD Outcome RR=relative risk**
Chun et al., 1984 (13)	Children (age 4-18) of Hawaiian descent	Observational study 1976-1980 School-based throat culture program for	No data on who funded and administered program	Control group: 29 cases of RF per 1,949,690 person-years.

		children with URTI symptoms in 60% of Oahu's public schools	Samoan distrust of Western medicine, seek medical help once home remedies and healers failed. - Samoan in low SES, overcrowded homes	Intervention: 36 cases of RF per 353,936 person-years RR=0.68 (95% CI, 0.42-1.12)- calculated by Heart foundation (4)
Coulehan et al. 1982 (14)	School children aged 5-16 years in the Navajo reservations in Wyoming, New Mexico, Arizona, Colorado, United States	Observational study from 1975-79 (51 months). Review of health records from Indian Health Service or private hospitals serving the Navajo community. No blinding, no randomization. School based sore throat clinic, run by nurses. Periodic throat swabs (every 4-5 months) from symptomatic and	Differences in schools funded by public and Federal Indian Affairs. Inconsistent throat swabs due to children's absenteeism, and personnel and transportation restraints to community sites. Improved access to health care to remote communities	30 cases of ARF diagnosed. In 29 of those cases, the school was determined: 7/29 attended schools with intervention, 22/29 of other ARF patients were in schools with no intervention. Less frequent ARF in participating schools. RR=0.39 (95% CI, 0.1-0.94)

		asymptomatic children. Penicillin treatment if GAS positive		
Lennon et al. 2009 (1)	South Auckland, New Zealand-Maori and/or Pacific students	RCT method clear. 1998-2001 Children with sore throats swabbed in schools. If GAS positive, treatment of penicillin administered at school 22,000 school children (5-18 years), half in treatment schools, half controls (no school clinics), followed for 4 years	School-based sore throat clinic. Direct access to health care Free nurse-observed oral penicillin treatment of GAS pharyngitis Parental and school consent obtained	1992 Jones Criteria and Echo to confirm ARF 28% reduction of ARF-26 cases in intervention (59/100,000) and 33 cases in control (77/100,000), (P=0.27).
Nicolle et al. 1990 (12)	School children from	Intervention study. No blinding. Randomization	HCP visiting schools Unclear how many children were involved.	RR not calculated

	Ranken Inlet, NU, and St. Therese Point, MB, Canada	method not clear. HCP visited the schools 3 times weekly to identify children with pharyngitis or skin lesions, and parents asked to consent to the randomization of IM or PO penicillin	Little detail on intervention.	Many children lost to follow up. No mention of rheumatic fever cases
Nordet et al., 2008 (15)	1986-1996 Included all 5-25 year old in the Pinar del Rio Province, Cuba	Observational study. No blinding or randomization Pilot study- incorporated primary and secondary ARF prevention program, training of personnel, health education, community	Community health education (pamphlets, posters, special media broadcast) Primary prevention- early and correct treatment of sore throats/GAS pharyngitis. Did not explicitly indicated method of diagnosing sores throat,	RR=0.08 (95%CI,0.02, 0.34) Decline in occurrence and severity of ARF. Decrease in the prevalence of RHD in school children from 2.27 per 1000 children in 1986 to 0.24 per 1 000 in 1996.

		involvement, epidemiological surveillance Cross-sectional studies at start and end, of all schools using "multi-stratified random-sample method"	only indicated use WHO RF guidelines (throat swab). Secondary prevention-secondary antibiotic prophylaxis, echocardiography to find cases of RHD and surveillance,	Reduction in registered cases of heart failure and heart valve surgery due to RHD. Multiple interventions run at same time, difficult to distinguish which had most effect.