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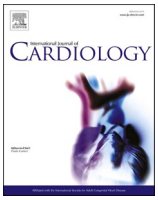

Follow-up echocardiographic changes in children and youth aged <25 years with latent rheumatic heart disease: A systematic review and meta-analysis of global data.

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ABSTRACT

Objectives: To estimate progression, regression and persistence rates for *borderline* and *mild-definite* latent RHD in children and youth diagnosed at age < 25 years.
Methods: A review was conducted in accordance with Preferred Reporting Items for Systematic reviews and Meta-Analysis guidelines. Electronic databases were searched for latent RHD echocardiography follow-up studies which used World Heart Federation diagnostic criteria. A meta-analysis of outcomes was conducted for *borderline* and *mild-definite* disease subcategories.
Results: Data for 1618 individuals from 12 studies were included. For *borderline* cases, 48.51% regressed (95%CI 45.10–51.93), 13.99% progressed (95%CI 9.72–18.25), and 38.61% had persistent (unchanged) disease at follow-up (95%CI 29.68–47.54). For *mild-definite* cases, 34.01% regressed (95%CI 28.88–39.15), 8.06% progressed (95%CI 3.65–16.90), and 60.23% had persistent disease (95%CI 55.08–67.38).
Conclusions: Borderline and *mild-definite* latent RHD show variable evolution following initial diagnosis. While 8% of *mild-definite* and 14% *borderline* cases had signs of disease progression at follow-up, a third of *mild-definite* and half of *borderline* cases had disease regression, even with sub adequate antibiotic prophylaxis. The significant variability between study cohorts suggests latent RHD natural history is likely variable between different endemic regions globally. Future research is needed to identify those individuals who would most benefit from antibiotic prophylaxis and determine regional natural history of latent RHD.

1. Introduction

Rheumatic heart disease (RHD) is the chronic sequela of acute rheumatic fever, an autoimmune response to *Streptococcus pyogenes* (Strep A) pharyngitis, with increasing evidence that Strep A skin infection can also a trigger acute rheumatic fever (ARF). [1] A severe or recurrent episode of ARF can lead to progressive RHD, characterised by lasting damage to the heart valves, resulting in morbidity and premature death. In 2019, global RHD cases were an estimated 40-million, [2] and while low to middle income countries have the highest disease prevalence, some of the highest rates of ARF/RHD are reported in Indigenous populations of high-income countries such as Australia and New Zealand, where RHD has become rare in the broader population. [3,4]

Disease prevention and control strategies range from reducing exposure to Strep A (primordial prevention), early diagnosis and treatment of Strep A pharyngitis and skin infection with antibiotics (primary

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prevention) and preventing RHD progression through recurrent ARF with active case-detection and antibiotic prophylaxis (secondary prevention). Active case-detection using echocardiography in community and school settings has identified a considerable number of children and young people with clinically silent (latent) RHD.

In 2012, the World Heart Federation (WHF) introduced new echocardiographic diagnostic criteria that provided increased sensitivity for latent RHD detection and classification into three categories of disease state, including *normal*, *borderline,* and *definite* (further categorised into *mild, moderate, and severe*). [5] The criteria have since become the gold standard for diagnosis and classification in young people without a prior record of ARF.

Early detection of *borderline* RHD and *definite* RHD (collectively referred to as either *screen-detected*, *subclinical*, or *latent* RHD) through active school and community case-detection has heralded a promising opportunity for early intervention, particularly following landmark findings of the GOAL trial (GwokO Adunu pa Lutino Trial: Determining the Impact of Penicillin on Latent Rheumatic Heart Disease). [6] The GOAL trail was the first randomised-controlled trial to evaluate the efficacy of benzathine penicillin G (BPG) prophylaxis for both *borderline* and *mild definite* latent RHD (over 2-years), demonstrating a significant reduction in the risk of disease progression for the latent RHD intervention group prescribed monthly antibiotic prophylaxis (adherence 99.1%), compared to the latent RHD control group who received no intervention. [6] Previously, the efficacy of BPG prophylaxis for latent RHD was uncertain. This new evidence led to an amendment of Australian RHD guidelines, [1] now recommending an intramuscular BPG every 28 days for children and youth diagnosed with *borderline* latent RHD for a minimum of 2-years. The results have also raised the interest of policy and decision makers in considering targeted RHD screening programs in endemic areas.

Ascertaining a clear understanding of the natural history and course of latent RHD has been challenging. Studies reporting rates of progression, regression, and persistence (unchanged) at follow-up show conflicting results, with some reporting *mild-definite* latent RHD is stable or reversible over time, [7,8] but others reporting significant rates of progression to *severe-definite* disease or death at follow-up. [9–12] In addition, study of latent RHD natural history is made difficult by the variable prescription of and adherence to antibiotic prophylaxis among studies. Given a fundamental requirement of screening is an adequate understanding of latent RHD natural history, [13] this review aims to summarise the current literature on follow-up rates of latent RHD regression, persistence, and progression with a meta-analysis of proportions.

Two previous meta-analyses have reported pooled estimates of RHD progression between 7.5% [14] and 15% [15] at follow-up echocardiography, and a >3-fold increased risk of progression for latent RHD cases compared to healthy controls. [15] Of the study cohorts used to base these estimates, 6 of 9 in the Noubiap et al. [14] review, and 8 of 12 in Gutman et al. [15] review, used the WHF echocardiographic diagnostic criteria. Further research restricted to studies (i) using the WHF criteria for consistency of classification is required, and (ii) focussing on two earliest subclinical manifestations of latent RHD (*borderline* and *mild-definite)*, since treatment for these patient groups remains a source of clinical equipoise in some settings and clearer recommendations for early intervention are needed. [5,16]

The research questions for this review were: (1) "What proportion of children and youth aged <25 years at first diagnosis of *borderline* or *mild-definite* latent RHD will have progression, remission or persistence at follow-up echocardiography?", and (2) "Do individuals with a diagnosis of latent RHD have higher risk of progression at follow-up compared to community peers with an initially *normal* diagnosis?" The primary outcomes of this study were: (1) pooled follow-up proportions of progression, regression and persistence for latent *borderline* versus *mild-definite* RHD; and (2) pooled risk ratios of follow-up disease progression for individuals with latent RHD (*borderline* and *mild-definite*) compared to controls (community peers with an initial diagnosis of *normal*).

2. Methods

2.1. Design and registration

This systematic review and meta-analysis was conducted in accordance with recommendation for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). [17] The study protocol is registered with PROSPERO [CRD42022318161].

2.2. Initial search strategy and eligibility criteria

Initial searches were conducted in March 2022, in five electronic databases (PubMed**,** Cochrane Library**,** Embase**,** Scopus, and CiNHAL). Search strategies for each database are outlined in **Supplement 1**. Secondary searches included manual searches of the reference lists of all included articles and prior systematic reviews involving follow-up of individuals with latent RHD.

2.3. Eligibility criteria

Studies were eligible for inclusion if they reported original RHD follow-up data for cohort members who: (1) were diagnosed with either *borderline* or *mild-definite* latent RHD; (2) were age < 25 years at baseline screening; (3) had no confirmed diagnosis of ARF or RHD prior to baseline screening; (4) were screened at baseline and follow-up using echocardiography and classified using WHF criteria; and (5) received at least one follow-up assessment after a minimum 18-month interval where numbers of disease progression and/or regression according to WHF criteria were a reported outcome. Eligible study types included prospective cohort, and standard or non-standard randomised-controlled trial designs (Sackett Levels of Evidence I-III). [18]

The 2012 WHF criteria are intended for use in people aged ≤20 years. However, separate criteria are included for people aged >20 years as screening may be justified, particularly for socially vulnerable in high-prevalence regions. Therefore, we decided on an upper age eligibility limit of 25 years to allow for studies that included some older people.

Studies were excluded if they: (1) were not in English language and in full text; (2) reported prevalence only with no follow-up; (3) classified cases using criteria other than WHF; (4) had a cohort which was present in a more recent study, in which case the more recent data was reported; (5) data for baseline cases younger than 25 years were not reported separately; (6) and data from *borderline* and *mild-definite* cases were not reported separately from *moderate-* and *severe-definite* latent RHD cases (Fig. 1).

2.4. Study selection

Studies were imported into Endnote (software) and duplicates removed. Remaining studies were then imported into Covidence for screening. Studies were screened by three separate authors, firstly based on title and abstract (CF, JC), then by full text review (CF, JC, SM). Divergent decisions were resolved by a third author (LJ).

2.5. Data extraction and management

The following data was extracted for each study: (1) citation (authors, title, and year of publication), (2) study methodology (design, randomisation, blinding of follow-up echocardiography evaluation), characteristics of study participants (country, age, gender), echocardiography (follow-up timeframe, total number screened, number of cases available at follow-up with both initial and follow-up diagnoses), and antibiotic prophylaxis, if provided (which subgroup(s) were prescribed prophylaxis at baseline, definition of prophylaxis adherence, proportion

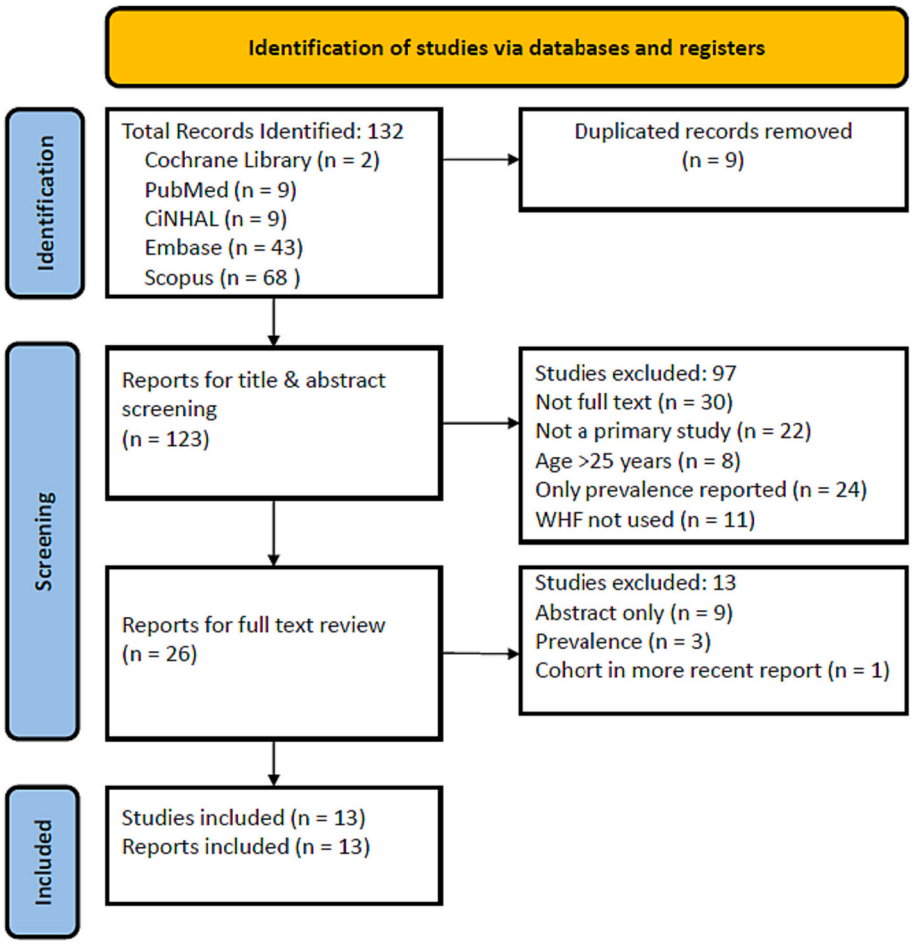

Fig. 1. PRISMA.
Flow diagram showing process of study identificationa and screening in accordance with Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.
RHD = rheuamtic heart disease.

adherent), (3) RHD data (baseline and follow-up classification for both patients with latent RHD and control groups where available). Data extraction was performed independently by three authors (CF, JC, SM) using a standardized form, and disparities were discussed until a consensus was reached.

2.6. Data synthesis and analysis

A meta-analysis of proportions was conducted. Extracted cases of latent RHD were separated into *borderline* or *mild-definite* at baseline (total cases), and corresponding follow-up outcomes of either progressed, regressed or persistent were combined in a random-effects meta-analysis using R (version 4.2.0, packages metfor version 3.8–1 and meta 6.0–0). Pooled proportions and associated 95% confidence intervals were calculated. In addition, prediction intervals were estimated to provide a range of expected proportions of disease progression, regression and persistence for 95% of settings.

To best approximate natural history, the GOAL trial [6] intervention group which had excellent prophylaxis coverage (99.1%), was excluded from pooling to reduce the influence of antibiotic prophylaxis on summary estimates. However, the GOAL trial [6] control group, a true latent RHD natural history cohort prescribed no antibiotic prophylaxis over a 2-year follow-up period, was included in pooling with data from other studies, serving as reference for disease progression without influence of antibiotic prophylaxis.

Heterogeneity was assessed using the I^2 and τ^2 statistics, and an explanation of heterogeneity was attempted through removal of significant outliers and moderator analysis. Outliers were identified through visual inspection of forest plots. Formal testing was performed by screening external studentised residuals and using the leave-one-out method, and significant outliers were removed. [19] Moderator analysis with meta-regression was also performed in an attempt to further explain heterogeneity among studies, including univariate analyses of two potential moderators 'prophylaxis adherence' and 'median follow-up', using mixed-effects models. [20]

Lastly, pooled risk ratios were calculated using data extracted from prospective cohort studies with healthy age- and sex-match controls. Risk of an 'unfavourable' outcome was defined as disease progression at follow-up, whereas a 'favourable' outcome was defined as either disease absence, regression, or persistence.

2.7. Quality appraisal

Two risk-of-bias tools were adopted to assess study quality. For prospective cohort studies, a modified risk of bias tool for prevalence studies developed by Hoy and colleagues was used. [21] For standard and non-standardized randomised-controlled trials, the Cochrane risk-of-bias tools for randomised-controlled trials (RoB2) was used, including additional considerations for cluster-randomised trials. [22] Assessment for publication bias was assessed using funnel plots and Egger bias test, with possible bias indicated with a p-value <0.05. [23]

3. Results

3.1. Search results

Initial searches identified 132 studies, of which 13 were eligible for inclusion in our review (Fig. 1). Of the 13 included studies, 11 were of a prospective cohort design, one was a cluster randomised trial, and one was a randomised-controlled trial.

3.2. Descriptive characteristics

A summary of the characteristics of included studies is presented in Table 1. The 13 included studies followed up a total of 1618 individuals with a diagnosis of either *borderline* ($n = 1209$) and *mild-definite* ($n = 409$) disease at baseline screening. All but one study had already excluded *moderate* and *severe* grades of *definite* latent RHD from follow-up ($n = 21$). [10]

From this study, we extracted only the *mild-definite* latent RHD cases for analysis. The median age of participants at initial diagnosis varied between 10 and 14 years (range 5 to 20). The median follow-up varied between 23 and 112 months (range 13 to 123 months). The proportion of female participants in studies ranged from 41% to 68%. The proportion of cases with adequate BPG coverage varied among study cohorts, including almost complete (99.1%, 1 cohort), majority (58% to 83%, 4 cohorts), poor (24% to 2%, 7 cohorts), and no antibiotic prophylaxis (2 cohorts). A total of 11 countries were represented, including five African, three South-East Asian, three Western Pacific, one Eastern Mediterranean, and one of the Americas as per the WHO regions. Of the three Western Pacific studies, there was a single Australian study, and none were from New Zealand. [9]

3.3. Risk of Bias

The risk of bias of 11 prospective cohort studies is summarised in

Table 1
Characteristics of included studies reporting on latent rheumatic heart disease follow-up.

Study	Country	Study design	Screened (number)	Total Female (%)	Median or mean age at initial diagnosis (years)	Median duration of follow-up (months)	Number of cases available at follow-up and baseline diagnosis		Antibiotic Prophylaxis		
							Borderline (number)	Definite (number)	Subgroup(s) offered antibiotics	Proportion of adherent cases (%)	Definition of adherence
Beaton (2022) Intervention	Uganda	RCT	102, 200	57	12.6	24	318	81	Definite & Borderline	99.1	≥80% days covered or ≥ 80% injection received
Beaton (2022) Control	Uganda	RCT	102, 200	54	12.5	24	333	67	Not applicable	0	Not applicable
Choudhary (2021)	India	PC	3000	40.6	12.5	24	3	42	Definite & Borderline	poor	Not stated
Gemechu (2021)	Ethiopia	PC	987	54	17.0	56.4	10	26	Definite & Borderline	5.6	Not stated
Karki (2021)	Nepal	CRT	3973	50.6	12.1	51.6	4	7	Definite only	75	2 doses of BPG or an alternative antibiotic in the 3-months before follow-up
Shrestha (2021)	Nepal	PC	5178	64.2	11.0	22.8	14	30	Definite only	58.3	2 doses of BPG or an alternative antibiotic in the 3-months before follow-up
Bechtlufft (2020)	Brazil	PC	541	65.7	14.0	28	170	27	Discretion of the treating Doctor	6.6	Received >80% of prescribed doses
Sanyahumbi (2019)	Malawi	PC	1450	55	9.97	24	36	11	Definite only	18	Received >80% of prescribed doses
Beaton (2017)	Uganda	PC	1715	60.4	12.0	28.8	164	42	Discretion of the treating Doctor	82.4	≥80% days covered or ≥ 80% injection received
Bertaina (2017)	New Caledonia	PC	8694	68	9.8	23	25	Not applicable	Borderline only	24[a]	Not stated
Kotit (2017)	Egypt	PC	3062	41.3	10.0	42.1	26	46	Definite & Borderline	83.3	Not stated
Engelman (2016)	Fiji	PC	134	67	10.4	90	17	20	Definite only	2	Received >80% of prescribed doses
Zühlke (2016)	South Africa	PC	2720	58.9	13.0	60.8	34	10	Not stated	4.6	Not stated
Rémond (2015)	Australia	PC	119	59	13.7	42	55	Not applicable	Not applicable	0	Not applicable

RCT = Randomised Controlled Trial; CRT = Cluster Randomised Trial; PC = Prospective Cohort.
Table showing the characteristics of each study included in the review and cases followed up categorised into latent rheumatic heart disease categories of interest: *borderline* and *mild-definite*. There are also details of antibiotic prophylaxis prescription and adherence among study cohorts.

Supplement 2. Eight studies [7–11,24–26] demonstrated a low risk-of-bias, and three studies [12,27,28] demonstrated a moderate risk-of-bias with respects to the external validity, including some concerns for non-response bias and sampling bias. The risk of bias of the randomised-controlled trial [6] (Low overall risk) and cluster randomised trial [29] (High overall risk) are summarised in **Supplement 3**. Due to the high risk of bias identified in the cluster randomised trial, [29] its data was excluded from meta-analysis. Egger tests showed significant funnel plot asymmetry which indicated that publication bias based on sample size was not likely.

3.4. Pooled proportions of progression, regression, and persistence

For cases with *borderline* RHD at baseline, the total proportion of disease progression at follow-up was detected in 13.99% of cases (95%CI 9.72–18.25; 11 studies; I^2 = 52%; Fig. 2). Regression from *borderline*

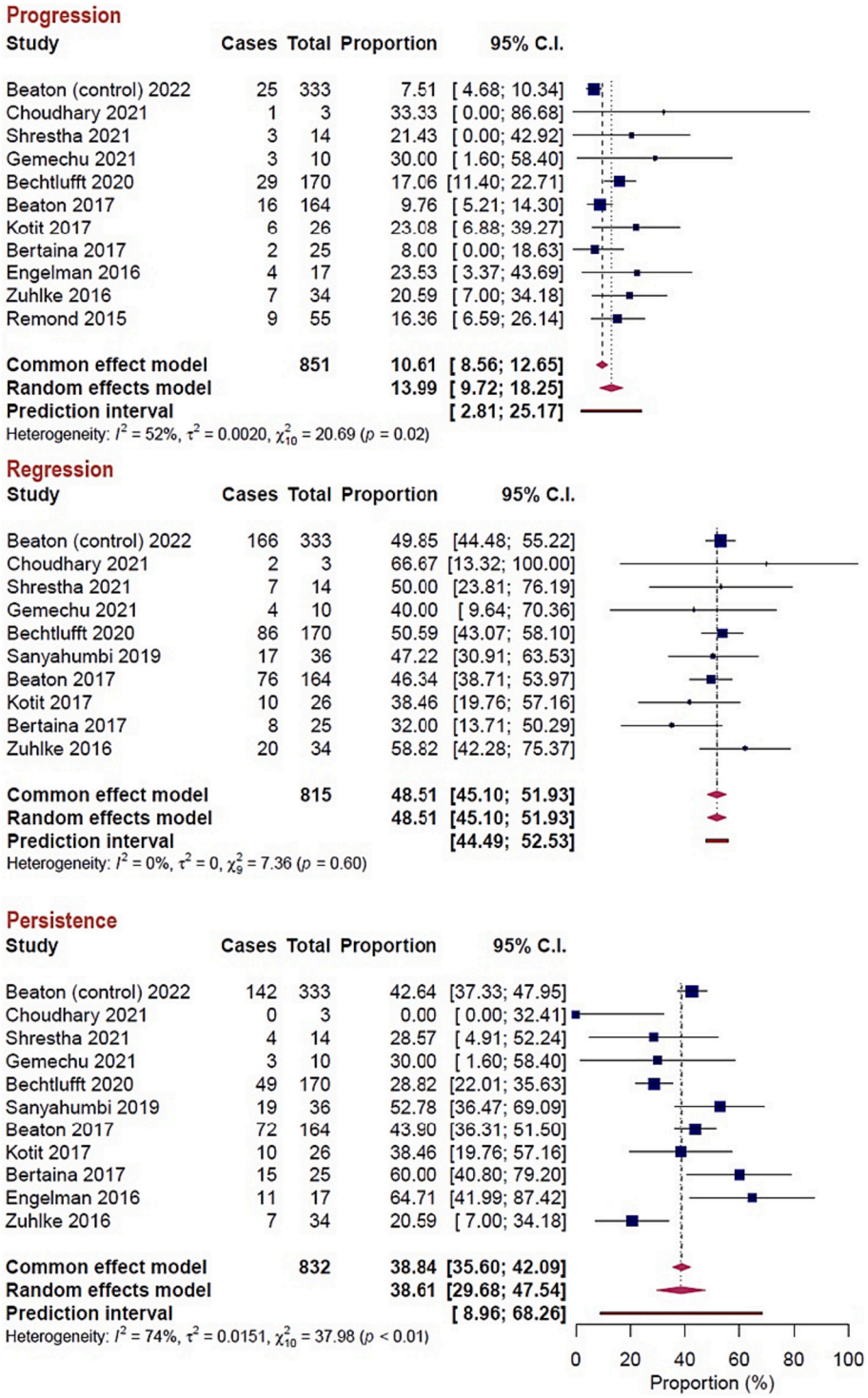

Fig. 2. Borderline latent rheumatic heart disease progression, regression, and persistence. Forest plot of meta-analysis including studies reporting proportion of *borderline* cases with echocardiographic evidence of disease progression, regression, and persistence (unchanged diagnosis) at follow-up according to 2012 World Heart Federation criteria.

disease to *normal* was detected in 48.51% (95%CI 45.1–51.93; 10 studies; $I^2 = 0\%$; Fig. 2). Persistent *borderline* disease was detected in 38.61% (95%CI 29.68–47.54; 11 studies; $I^2 = 74\%$; Fig. 2).

For cases with *mild-definite* RHD at baseline, disease progression at follow-up was detected in 8.06% of cases (95%CI 3.65–16.9; 10 studies; $I^2 = 58\%$; Fig. 3). Disease regression was detected in 34.01% (95%CI 28.88–39.15; 10 studies; $I^2 = 0\%$; Fig. 3), and the prediction interval ranged from 27.97 to 40.06%, with 95% confidence. Persistent *mild-definite* RHD was detected in 60.23% (95%CI 55.08–67.38; 9 studies; $I^2 = 26\%$; Fig. 3).

Outliers were removed from *borderline*-progression (Sup. 4.1a), *borderline*-regression (Sup. 4.2a), and *mild-definite*-persistence models (Sup. 4.3a). This resulted in the reduction of between-study heterogeneity of each model to insignificant levels and narrowing of corresponding prediction intervals (Sup. 4.1b; Sup. 4.2b; Sup. 4.3b). Univariate meta-regression did not explain the remaining heterogeneity among studies in *mild-definite*-progression and the *borderline*-persistent models from potential moderators: 'prophylaxis adherence' (range: 0% to 83.3%), or 'median follow-up' (range: 22.8 to 60.8 months).

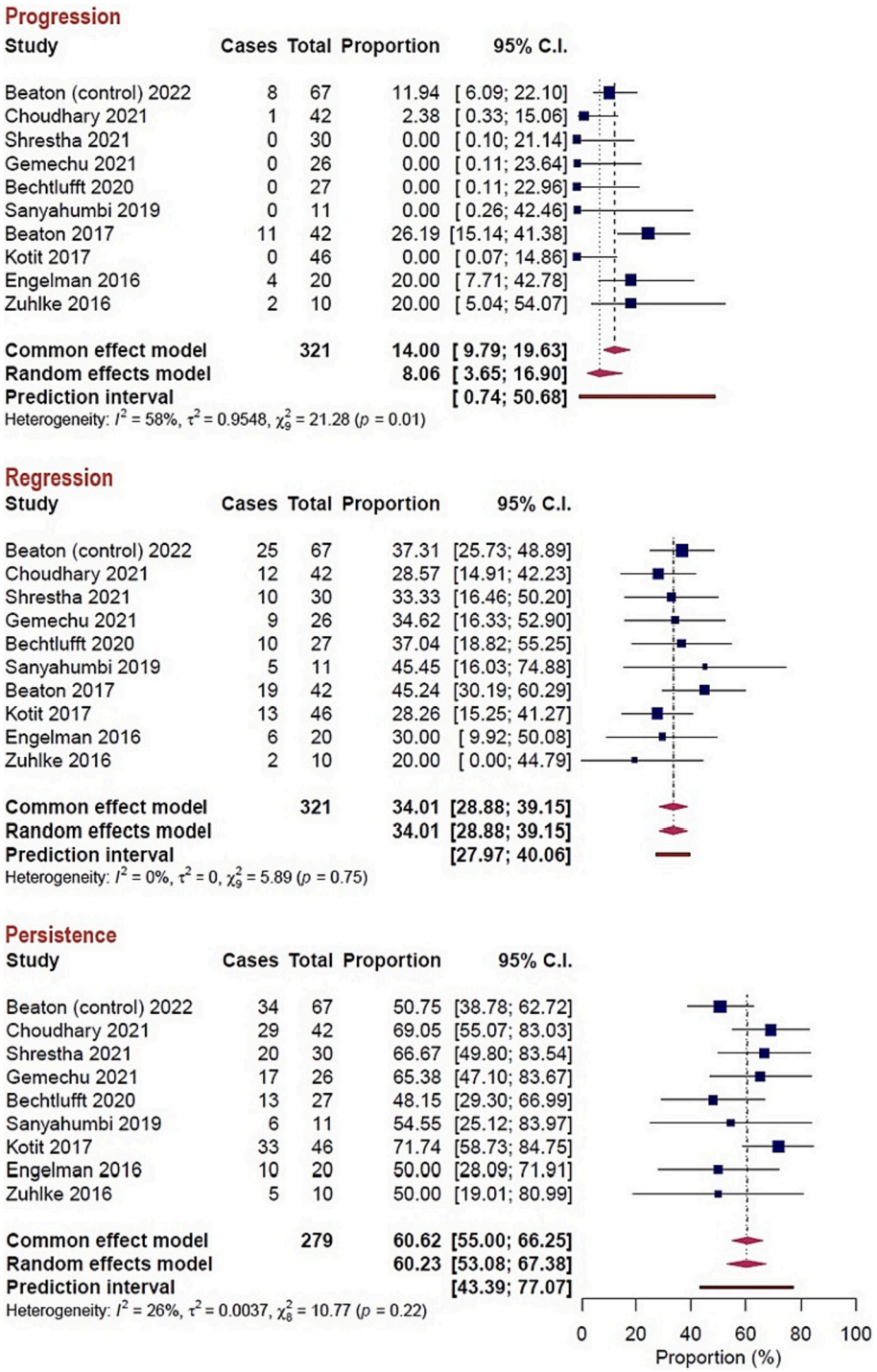

Fig. 3. Mild-definite latent rheumatic heart disease progression, regression, and persistence. Forest plot of meta-analysis including studies reporting proportion of *mild-definite* cases with echocardiographic evidence of disease progression, regression, and persistence (unchanged diagnosis) at follow-up according to 2012 World Heart Federation criteria.

3.5. Risk of progression

Pooled risk ratio of disease progression at follow-up for individuals diagnosed with latent RHD (combined *borderline* and *mild-definite* cases) compared to controls (community peers with an initially *normal* diagnosis) included data of four prospective cohort studies with control groups (Sup. 5). [9,12,26,28] Antibiotic prophylaxis was not prescribed in Rémond et al. [9] and adherence was variable between the three remaining studies, in which prophylaxis was prescribed (range: 2% to 83.3%). The mean or median follow-up interim varied between 40 and 90 months. Subgroup analysis of *borderline* and *mild-definite* groups was not possible due to insufficient data.

For pooled studies, [9,12,26,28] the summary estimate of relative risk of an 'unfavourable' follow-up outcome (disease progression) was statistically insignificant as the 95% confidence interval contained the null value (RR 1.95 [95% CI 1.00–3.80]; 4 studies; $I^2 = 42\%$; Sup. 5). While Rémond et al. [9] and Engelman et al. [12] report a higher risk of an 'unfavourable' outcome for individuals with latent RHD compared to controls, Kotit et al. [26] and Gemechu et al. [28] showed risk to be equivocal between the two groups. Further attempts to explain heterogeneity through meta-regression was not possible due to small number of studies.

4. Discussion

This review presents the most contemporary estimates of *borderline* and *mild-definite* latent RHD echocardiographic follow-up outcomes. Data involved >1600 children and youth, using the consistent gold standard WHF echocardiographic diagnostic criteria. These estimates were based on data from 12 study cohorts, including data from seven studies published since the previous review. [15]

Our analysis indicates that 14% of people with *borderline*, and 8% with *mild-definite* latent RHD had signs of disease progression at follow-up (Fig. 2; Fig. 3). However, for most children and youth, follow-up echocardiography results at a minimum of 23 months were either unchanged (*borderline*: 39%; *mild-definite*: 60%) or showed improvement (*borderline*: 49%; *mild-definite*: 34%). Previous reviews have reported lower estimated rates of progression and regression, and higher estimated rates of persistence for both *borderline* and *mild-definite* latent RHD subgroups. [14,15] These estimates fell within our generally narrower prediction intervals in each model, which likely reflects the improved precision of our estimates given our additional case data.

Recent evidence for the benefit of BPG prophylaxis for latent RHD has added further justification towards a population-based echocardiographic screening approach in endemic regions. [6] However, access to antibiotic prophylaxis and adherence remains a significant challenge for RHD control and prevention globally. [25,27,28] The robust antibiotic adherence in the GOAL trial (99.1%) was achieved through highly effective but costly strategies (travel reimbursement, use of case-managers and peer support groups) to overcome the many real-world barriers to levels of adequate adherence (≥80% of prescribed BPG doses). [6] Prior to implementing this model of screening at scale, health-system considerations such as need, cost, resource allocation, and competing public health priorities must be considered. It is essential there is adequate funding, community support, and resources available for the delivery of care. Practical and sustainable solutions for patient retention in follow-up care is needed to ensure potential for adequate adherence is in place before implementation of a screening program. Further research is needed to evaluate the cost-effectiveness of RHD screening to build a case for health system investment.

Australian guidelines currently recommend that children with an initial diagnosis of *borderline* RHD receive an intramuscular BPG injection every 28-days for a minimum of two years. [1] For *mild-definite* RHD, monthly BPG injections are recommended for a minimum of five to 10-years, depending on whether a record of previous ARF exists. [1] Currently, it is not possible to predict which *borderline* and *mild-definite* RHD cases are more likely to regress or progress without treatment with BPG. A simple risk score based on features of echocardiography identified on diagnosis and tested prospectively on a cohort of Brazilian school children over two years, had demonstrated good performance in discriminating cases likely to progress, but these findings have not been reproduced in other populations. [25] Given that an estimated one third of *definite* cases and half of *borderline* cases regress at follow-up without the influence of antibiotic prophylaxis, it is understandable that there remains uncertainty regarding the most appropriate clinical management of these children and youth. Future research is needed to better understand risk of progression, to help mitigate the harm to many children and youth diagnosed with latent RHD, for whom BPG is not of benefit.

A fundamental requirement of RHD screening is an understanding of disease natural history. [13] While the pooled estimates in this review provide some guidance on likely disease evolution in regions without follow-up studies, there is variability across different study regions. For endemic areas, an analysis of local data is necessary to understand the place specific latent RHD natural history of the region. This information is valuable to establish need and advocacy within health systems for appropriate allocation of resources. While data in this review were sourced from the scientific literature, RHD registers are also a source of data which can be used to describe region-level natural history. [30] Future research should evaluate regional RHD register data linked with health and administrative data to better understand early latent RHD natural history, including analyses of risk associated with disease progression.

The main limitation of our study was the inclusion of only one randomised-controlled trial. The remaining prospective cohort studies are prone to bias inherent to their study design, albeit these demonstrated low to moderate risk. Other limitations include small sample sizes, short follow-up duration, and variable prophylaxis adherence between included studies which impacted our analysis of progression risk for latent RHD compared to controls. Further to this, a separate analysis of *borderline* cases versus controls was attempted to explore the significance of *borderline* RHD as a clinical subgroup but was not possible due to small numbers.

5. Conclusion

In conclusion, *borderline* and *mild-definite* latent RHD when diagnosed in children and youth aged <25-years have variable natural history that ranges from disease progression, regression, or persistence. Although new evidence supports the efficacy of antibiotic prophylaxis to prevent lesion progression, adding justification to population-based screening, over half of lesions resolve spontaneously without pharmaceutical intervention in an unknown subset of children and youth. Future research is needed to identify those individuals who would benefit the most from antibiotic prophylaxis. In addition, RHD register data may be used to determine regional natural history as well as establish local needs and health system advocacy.

CRediT authorship contribution statement

Carl J. Francia: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Validation, Visualization, Writing – original draft, Writing – review & editing. **John F. Fraser:** Conceptualization, Resources, Supervision, Writing – review & editing, Writing – original draft. **Robert Justo:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing. **Joan Cassimatis:** Data curation, Writing – original draft, Writing – review & editing. **Sophie Manoy:** Data curation, Writing – original draft, Writing – review & editing. **Leanne M. Johnston:** Conceptualization, Data curation, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2024.131911.

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