Standardizing clinical care measures of rheumatic heart disease in pregnancy: a qualitative synthesis

Abstract

Background: Rheumatic heart disease (RHD) is a preventable cardiac condition that escalates risk in pregnancy. Models of care informed by evidence-based clinical guidelines are essential to optimal health outcomes. There are no published reviews that systematically explore approaches to care provision for pregnant women with RHD and examine reported measures. The review objective was to improve understanding of reporting of attributes of care for these women and how they align to guidelines.

Methods: A search of 13 databases was supported by hand-searching. Papers that met inclusion criteria were appraised using CASP/JBI checklists.

A content analysis of extracted data from the findings sections of included papers was undertaken, informed by attributes of quality care identified previously from existing guidelines.

Results: The 43 included studies were predominantly conducted in tertiary care centers of low-middle-income countries.

Cardiac guidelines were referred to in 25/43 studies. Poorer outcomes were associated with higher risk scores (detailed in 36/41 quantitative studies).

Indicators associated with increased risk include anticoagulation during pregnancy (28/41 reported) and late booking (gestation documented in 15/41 studies). Limited access to cardiac interventions was discussed (19/43) in the context of poorer outcomes. Conversely, early assessment and access to regular multidisciplinary care was emphasized in promoting optimal outcomes for women and their babies.

Conclusions: Despite often complex care requirements in challenging environments, pregnancy provides an opportunity to strengthen health system responses and address whole-of-life health for women with RHD. A standard set of core indicators is proposed to more accurately benchmark care pathways, outcomes and burden.

Keywords: Health Care Quality, Access, and Evaluation; Pregnancy; Rheumatic Heart Disease; Social Determinants of Health; Systematic review, Best practice

Abbreviations: CARPREG CARdiac disease in PREGnancy risk score; **NYHA** New York Heart Association functional class (I-IV); **CDiP** Cardiac disease in pregnancy; **RHD** Rheumatic heart disease; **RHD-P** RHD in pregnancy;

Key message/Tweetable abstract

Key reporting measures in studies that include rheumatic heart disease in pregnancy are often poorly recorded. We can do better. A core dataset proposed to more accurately benchmark care pathways, outcomes and burden of RHD in pregnancy.

Standardizing clinical care measures of rheumatic heart disease in pregnancy: a qualitative synthesis

Introduction

Rheumatic heart disease (RHD) is a preventable disease of inequity. It is twice as common in women[1-4], creating added risk in pregnancy. There are many challenges to providing optimal care for women with RHD, particularly in low-and-middle income countries. Service provision is limited by poorly-resourced expertise and facilities with barriers of distance and cost. There is often deficient awareness for women and health services of RHD and its impact in pregnancy.

Consequently, the higher prevalence of RHD in pregnancy (RHD-P) in low-and-middle income countries is matched by poorer outcomes than in high-income countries, with documented maternal mortality rates of up to 37%[5]. Its burden is also high among vulnerable populations in upper-income countries. In Australia, Aboriginal and Torres Strait Islander women are over five times more likely to die from RHD[6], with RHD-P rates for Aboriginal Northern Territory women up to 63 times those of non-Indigenous women[7]. Inequitable outcomes are also seen in Māori and Pasifika women[8] and First Nation populations in North America[9,10]. There are growing numbers of women with RHD in high-income countries as migration from resource-poor countries increases[11,12].

There are no known systematic reviews that describe approaches to care and associated reporting measures for women with RHD-P globally. A review of the burden of antenatal cardiac disease in South Africa has a strong focus on RHD[13]. Guidelines refer to all-cardiovascular pathologies in pregnancy[14], or are referenced in non-pregnancy-specific cardiac valvular[15-17] or RHD-specific guidelines[4].

Reporting measures for studies of cardiac disease in pregnancy are currently in development[18] as part of the Core Outcomes in Women's and Newborn Health (CROWN) initiative[19,20], but there is no known equivalent for RHD-P, which has specific risks related to its epidemiology.

While clinical pathways can vary considerably according to the severity of RHD, principles of care that promote optimal maternal and baby outcomes include early diagnosis; preconception care including surgery and other interventions where required; early antenatal assessment including echocardiogram; access to specialized centers and treatment for high-risk women; and collaborative individualized care across disciplines and sectors[4,14,21].

The purpose of this study was to systematically examine descriptions of care provision and associated outcomes for women with RHD-P in order to improve the understanding of how attributes of care are reported and how they align with guidelines.

Methods

Due to the lack of internationally accepted RHD-P measures we reviewed relevant models of care and associated reporting measures referred to in clinical guidelines to conceptualize existing measures in a framework. We found no specific guidelines for RHD-P. Guidelines were chosen that addressed all-cardiac disease in pregnancy[14] and RHD with some reference to pregnancy[4].

The scope was further broadened to include cardiovascular care standards in primary health settings for Australian Aboriginal and Torres Strait Islander peoples[21]. This guideline outlines elements of care across the continuum of risk and disease, with a focus on reducing disparity in access and outcomes: applicable for most populations where RHD is disproportionate.

Reporting measures relevant for women with RHD-P were identified and grouped in three categories to provide an analytic tool with which to interrogate the literature (Figure 1).

These included: clinical information and reporting; risk in pregnancy; and RHD through the life-course. This framework served to guide the analysis of data gathered for the systematic review presented in this paper.

Data sources and search protocol

A structured search of peer-reviewed research literature identified studies that described clinical care and measures for women with RHD-P. Data were extracted from the reported results of included studies and examined using a content analytic process[22], directed by the framework of reporting measures (Figure 1).

The study was registered with the International Prospective Register of Systematic Reviews (PROSPERO #CRD42018059849).

Searches on PubMed, Medline, EMBASE, CINAHL, Nursing and Allied Health Database, ATSIhealth, Indigenous Collection, Rural and Remote Health Database, ETG Complete, ISI Web of Science, Public Library of Science and Trip Pro Databases; were supported by hand-searching. The search strategy incorporated a combination of free term text items and Medical Subject Headings (MeSH): ("rheumatic heart" or "rheumatic fever" or “valvular heart disease”) and ("pregnancy" or "pregnancy complications" or "pregnancy, high-risk" or "pregnancy complications, cardiovascular" "maternal") and ("models of care" or "guideline*" or "health service" or "maternal health services" or "primary health care" or "practice guideline" or "guideline adherence" or "health services accessibility" or "health care"). Inclusion criteria included: all English-language peer-reviewed studies after 1994 in any setting or country with reference to RHD-P and attributes of care (Table 1).

The PICOS framework (Population, Interventions, Comparators, Outcomes, Study design)[23] guided the review question: *In studies that reference pregnant women with RHD, what core reporting measures are used to describe models of care?*

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[24] informed the review. Screening utilized Endnote™ bibliographic and Covidence™review tools. Critical appraisal referenced CASP and JBI checklists[25,26] and the quality appraisal is summarized in Figure 4 as a four-tier grading. Differing judgments on inclusion were resolved by consensus, or, where no consensus was achieved, by a third reviewer. Reasons for excluding studies were clearly documented (Figure 2).

Data extraction and content analysis

A data extraction tool was developed using Microsoft Excel™. Visual mapping used Tableau™v2018.2.0 analytic software. Study characteristics included (Table 2, Figure 3) country, World Bank income category, study design, setting/s and population, as well as documenting maternal mortality. Data were coded against the reporting framework and associated measures (Figure 1).

Results

General characteristics and quality appraisal

The most common types of study design were cohort (19) and case-series (20), with two qualitative[27,28] studies, one cross-sectional[29] and one longitudinal screening study[30]. There was considerable heterogeneity in the methodologies, levels of evidence and reporting measures of these predominantly retrospective studies. Individual study characteristics are outlined in Table 2. Reflecting the overall burden of RHD, the majority of the 43 studies from 18 countries were from India (8), South Africa (6), Pakistan (4) and Thailand (4), with one multi-country (predominantly Egypt) study (Figure 3). Most were published after 2004, paralleling a resurged clinical and research interest[31]. The distribution of studies by country and World Bank income category is detailed in Figure 3.

All studies were conducted in tertiary care settings with access to cardiac (or dedicated obstetric-cardiac) care, as well as primary health settings[27,28,30] and regional centers[30,32].

Maternal mortality ranged from 0% (16/42) to 37%[5]. Between 1-4% of women died in nearly half (20) of the studies. One study found significantly lower mortality rates in its index population (10%) compared to referred women (32%)[32].

Study designs impacted on quality and were subject to high levels of bias, especially the case series. Referral and other selection biases as acknowledged in several papers[30,32-43] were particularly related to the predominantly single site tertiary care level settings.

Study periods ranged from six months to 21 years, with five of unspecified periods[39,44-47]. Long study periods (from 10-21 years in 16 studies) were noted to impact on protocols which changed in response to therapeutic advances during that time[33]. Figure 4 provides the quality appraisal overview and maps studies against reporting measures. The studies were assessed as low (9), medium (12), medium-high (21) and high (1) quality respectively. Key reporting measures from the framework (Figure 1) were poorly documented.

Clinical information reporting

The percentage of the study population with RHD ranged from 100% (11 studies of women with RHD or mitral stenosis) to 3% in a high-income country[11], with most comprising over 55% of the study population (Table 2). Six studies[29,46,48-51] from countries with an otherwise medium-to-high burden of RHD did not give a breakdown of underlying pathology of mitral stenosis or all-valvular heart disease(Table 2, Figure 4). Mitral stenosis in women during their reproductive years is usually of rheumatic origin[14,52] and was used as a proxy for RHD where causation was unspecified.

Heart disease in low-and-middle income countries is commonly diagnosed in pregnancy on development of severe symptoms[5,13,32,44,53]. However, 18 of the 41 quantitative studies did not specify timing of diagnosis. Others referred to late diagnosis in the context of poorer outcomes and health system shortcomings[35,40,41,49,51,54-56]. Diagnosis during pregnancy/post-partum ranged from 1%[57] to 97%[30] in a longitudinal screening study, with eight studies above

20% and four above 40%. In one high-income country, four women (of 95 pregnancies) were diagnosed with RHD after developing peripartum acute pulmonary oedema[58]. One found 7% of women diagnosed post-partum[39], but this was poorly documented overall.

Thirty-six studies specified echocardiographic review during pregnancy, although only four referenced diagnostic criteria[30,43,48,58]. Six studies did not specify RHD diagnosis confirmed by echocardiography, nor its use during pregnancy[5,46,53,59-61].

Models of care and risk in pregnancy

There was limited or no reference made to guidelines related to the care of pregnant women with cardiac disease in 16 studies.

The majority of the 36 quantitative studies that specified a cardiac risk score used the New York Heart Association (NYHA) classification (I-IV) of functional capacity[62]. Pregnancy-specific scores referenced CARdiac disease in PREGnancy (CARPREG)[63] cardiac events risk index, modified CARPREG[58], and modified World Health Organisation (mWHO) risk classifications[14,64]. A referral algorithm was developed for suspected and known cardiovascular disease in a low-resource setting[40].

Poorer maternal and fetal outcomes were associated with higher risk scores (NYHA>II[29,35,38,42,43,45-47,50,53-57,59,60,65-71], NYHA>I with mitral stenosis[43], mWHO>1[40], CARPREG[36,54,67,72]/modified CARPREG[58]>0 or study-specific factors such as mitral stenosis and anticoagulation therapy leading to increased maternal risks of heart failure, pulmonary hypertension, thromboembolic episodes, atrial fibrillation and death[30,32,37,41,46,48,49,51]). The CARPREG index underestimated cardiac events in low-risk women but over-estimated it in CARPREG>0 in one study, possibly reflecting late diagnoses in pregnancy[54]. The quality of care and avoidable factors associated with near-miss morbidity was assessed in two papers[32,41], while others described gaps between guideline recommendations and clinical implementation leading to compromised care[11,43].

Late booking and/or infrequent antenatal care hampered early diagnosis and treatment[5,49,59]and was associated with poorer cardiac and perinatal outcomes[32,40,41,49,51,67,69,70], yet the gestational age at first antenatal visit was reported in only 15 of 41 quantitative studies.

Medical management (such as beta-blockers, digoxin and/or diuretics) and Percutaneous Balloon Mitral Valvuloplasty[73] (PBMV, hereafter valvuloplasty) in refractory cases of mitral stenosis generally improved outcomes[33,34,56] where reported. However, studies emphasized the challenges of providing optimal care in resource-challenged environments, including appropriate clinician skills, access to medication, valvuloplasty and surgery, health system shortcomings and sociocultural factors[27,30,32,34,35,40,41,43,44,46,49,51,54-56,59], with one (where 37% of women with rheumatic valvular disease died) noting that valvuloplasty facilities were simply unavailable at their tertiary center[5]. The multi-country study found a greater number of valvular interventions in high-income countries despite more women in low-income settings having severe mitral stenosis[43].

Despite the potentially catastrophic maternal-fetal risks associated with the use of anticoagulation in pregnancy, the regimen was detailed in only half of the 28 quantitative studies that specified the number of women on therapy. Nine referred to discussion with women in the context of complex decisions surrounding choice of regimen which balanced the maternal risk of thromboembolism using low molecular weight heparin against the increased fetal risk of warfarin use. Studies discussed late booking affecting the anticoagulation regimen[47,51,66,70] with lack of adherence to protocol (or access to treatment) detailed as an important risk factor for morbidity and mortality[41,47,51,53,57]. Warfarin embryopathy/fetopathy was likely underestimated in studies where postmortems or detailed examinations were not performed[41,65].

Secondary prophylaxis (usually 3-4 weekly bicillin injections), where indicated, prevents rheumatic fever recurrence and is safe during pregnancy. Its use was referred to in only seven quantitative studies.

Most studies emphasized the need for multidisciplinary care in discussion and/or recommendations although somewhat fewer (32) specified its provision in their study. This was highlighted in one study that found obstetric-cardiac individualized review determined according to risk promoted optimal outcomes despite its low-resource setting[40]. Others similarly pointed to early multidisciplinary evaluation and management contributing to few or no maternal deaths in otherwise high-risk women[38,47,49,50,56,58,61,65,68,70,71].

Vaginal birth is recommended for women with valvular heart disease unless contraindicated by severe cardiac morbidity[14], or obstetric complications. Caesarean section rates varied enormously from less than 10%[44,46,50,61] to 75%[69], with several studies above 40%[35,41-43,47,57,68] and higher again in groups stratified by risk or poorer outcomes[42,43,57,68,69].

There was limited reference to care outside the index pregnancy period. Those that did noted the continued heightened risk of morbidity and mortality[40,43], and another detailed an increased need for cardiac intervention in the first year following delivery[11].

Papers that called for improved clinician training in primary health settings to support cardiac disease detection/referral[48,51,67] were mostly (5/6) published since 2014. Gaps in awareness among primary health care nurses (and women) were associated with delayed referrals[40] and consistent with other studies that found women received contradictory advice and limited education[27,28]. Language-appropriate health education that promoted a shared understanding was largely absent for Aboriginal women with RHD[28].

RHD through the life-course

Twenty-six studies did not specify the provision of conception counselling and reproductive health in their setting, with one listing it under management standards not followed[11]. Women can perceive risk to be over with the end of pregnancy[65], underscoring the significance of postnatal counselling.

Emerging themes in a qualitative study of women's experiences with RHD included misconceptions about side-effects of contraceptives; lack of agency in reproductive decision-making; and stigma related to financial and perceived reproductive limitations[27].

Discussion

The aim of this review was to synthesize the literature and map reported measures against a framework drawn from guidelines related to models of care for RHD-P. Our study found gaps in the three framework categories of clinical reporting, risk in pregnancy and RHD through the life-course.

A recent overview of RHD strategies emphasizes the imperative for accurate, current data in order to inform policy and measure trends[1]. Poor reporting of measures related to cardiac pathology and diagnoses precludes a true assessment of the burden of RHD-P and changing epidemiology. In turn, this is limited by the capacity of health services to diagnose cases. Women with subclinical or milder forms of disease or fatal events prior to admission are likely to be missed in low-income settings[40]. The community-based screening study found less than four percent of women with RHD were aware of their diagnosis pre-pregnancy[30]. There are no known studies of the impact of RHD-P from countries that have among the highest reported rates of RHD in the world[74], including the Pacifica[75,76] and Oceanic regions[77]. A population-based study conducted in the high-income countries of Australia and New Zealand (currently under review) shows similarly high rates among Māori and Pasifika women[8,78].

Reporting gaps are consistent with a South African systematic review of antenatal heart disease, which recommended minimum criteria including diagnosis, reference population, cardiac profile and outcomes[13].

While the lack of diagnostic reference to echocardiography is partly explained by study periods, resource limitations of facilities and expertise no doubt also impact. However, increasingly portable technologies and successful screening programs strengthen the argument for earlier review in primary care settings[30,79,80]. Standardization has improved with the 2012 echocardiographic diagnostic criteria[81].

The high risk of anticoagulation in pregnancy requires better reporting in any study of women with RHD. A recent meta-analysis of anticoagulation in women with mechanical heart valves found fetal risk was similar between women taking <5 mg warfarin daily to those on low-molecular weight heparin[82]. These findings underscore the need for granularity of reporting prescribed regimens – including level of adherence and whether women had access to treatment.

Increasing calls to improve the scale-up of and access to surgery/interventions in low-income countries[83,84] reflect service deficiencies highlighted in studies.

There were few studies that followed RHD-P care trajectories and outcomes outside tertiary centers. A small but growing number of initiatives such as the landmark RHD screening study[30] harness specialist resources in community settings to improve early diagnosis of RHD and care for women. These are embedded in collaborative cross-sectoral approaches[80], drawing on successful strategies developed in other chronic disease models and supported by strengthened health systems[30,85]. They potentially obviate the need for emergency-driven, costly tertiary care[32] - and in turn support improved outcomes for this disease which is preventable at many levels.[4] Such principles can equally apply to vulnerable populations in

high-income countries[86]. However, executing these models in practice is often tested by the plethora of structural, political and economic barriers to implementation that are part of the RHD landscape.

The overall lack of reference to post-discharge care (including recommended follow-up) suggests likely under-reporting of complications. Three of four RHD-related maternal deaths reported in the multi-country study were up to six months' post-partum[43], consistent with (often-avoidable) factors and risks reported in other studies of late maternal death[87-89].

Existing literature on preconception and reproductive health care is predominantly focused on congenital heart disease. There is a growing body of evidence of the role of preconception care in optimizing general health and risk awareness in marginalized communities[90]: highly relevant for women with RHD[3].

There are no RHD-P-specific guidelines. Selected reporting measures were drawn from cardiac disease in pregnancy guidelines that referenced RHD[14], the Australia-specific RHD guidelines[4,91] (an updated edition of which includes a substantially enhanced section on women and RHD[91]) and cardiovascular standards for Aboriginal and Torres Strait Islander peoples[21]. Guidelines are themselves mostly based on case series and observational studies. However, we believe the included reporting measures reflect fundamental principles of care for vulnerable populations where RHD is prevalent, particularly in relation to maternal health. RHD-specific research to test the evidence is required to strengthen the rigour of recommendations, better understand the effects of pregnancy and choose the best individualized plan for ongoing care.

We propose the reviewed framework of measures (Figure 1) addressing the categories of clinical information reporting; models of care and risk in pregnancy; and RHD through the life course as a core outcome set for women with RHD-P, adapted to local cultural, social and

economic contexts[92]. A Delphi method review[93,94] to evaluate an extended set with neonatal outcomes (with global stakeholders including health services and women in high-prevalence settings) will further strengthen recommendations for adoption.

Strengths and limitations

This review was constrained by the heterogeneity and design of included studies, with most subject to substantial bias (particularly referral) and reporting inconsistencies. Study sites were predominantly tertiary centers, providing care particularly for those with severe RHD who were able to access specialist care. However, these observational studies provide the best available current evidence and insight in determining models of care associated with optimal maternal outcomes.

What was reported (or not) may not reflect actual practice. In the absence of specific reference to a care attribute, it was assumed that it was not addressed, which may or may not be true. This may be particularly relevant for aspects such as conception counselling[11].

Conclusions

RHD has been described as providing a model for strengthening health systems to address other cardiovascular diseases in limited-resource countries. This framework is especially pertinent for women with RHD, where best-practice models of care in a strengthened maternal health system are often congruent with those that support women with RHD.

This qualitative synthesis highlights gaps of what is reported in the literature, with consequent under-estimation of burden and weakened ability to action strategies based on findings. We propose a Delphi testing of the reporting framework detailed in this paper and adoption of a core outcome set to support data consistency, comparability of studies, strengthen knowledge and awareness of burden (clinical and social) and improve benchmarking of care for women with RHD.

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Tables and figures

Table 1: Inclusion / exclusion criteria for content analysis of studies with reference to RHD-P

Included	Excluded
1995-2018	Pre-1995
English language	Non-English
Any setting in any country	None
Any study of women with cardiac disease with reference to RHD and pregnancy and attributes of care	Conference abstracts Opinion pieces/editorials Guidelines/reviews Systematic reviews Studies of biomedical treatments/interventions for women with RHD that do not refer to models of care in pregnancy

Table 2: Characteristics of studies with reference to RHD-P

Legend:

TCC: Tertiary care center; CR: Community setting and/or regional center

PCS: Prospective case-series; RCS: Retrospective case-series; PC: Prospective cohort; RC: Retrospective cohort; PLS: Prospective longitudinal screening

CDM: Dedicated Cardiac/Maternity clinic; HRPC: High-risk multidisciplinary pregnancy clinic

CDiP: Cardiac disease in pregnancy; VHD: valvular heart disease; MVHD: mitral valvular heart disease; MS: mitral stenosis

Maternal mortality: * Asterisked percentages indicate RHD only

	Study	Setting / Type of care	Study population	Study design	Country(s)	Objectives	Maternal mortality (rounded to nearest percent)
1	Abdel-Hady(2005)[57]	TCC-HRPC	n=86 RHD=90%	PCS	Egypt	Assess maternal/perinatal CDiP outcome.	1%*
2	Ahmed(2015)[48]	TCC-HRPC	n=101 RHD=N/S MS=100%	PCS	Pakistan	Evaluate MS feto-maternal outcomes, patient-specific management plan.	2%
3	Asghar(2005)[44]	TCC-HRPC	n=50 RHD=66%	PCS	Pakistan	Assess maternal/fetal outcome CDiP.	0%*
4	Avila(2003)[33]	TCC-HRPC	n=1000 RHD=56%	RCS	Brazil	Experiences & outcomes CDiP in referral center.	2%
5	Barbosa(2000)[34]	TCC-CDM	n=45 RHD=100%	RC	Brazil	Identify characteristics of complications MS in pregnancy.	2%*
6	Beaton (2018)	PLS, CR	n=58 RHD=88%	PLS	Uganda	Determine prevalence of maternal heart disease through active case finding & its attributable risk to adverse pregnancy outcomes.	2%*
7	Belton(2017)[28]	TCC-HRPC, CR	n=8 RHD=100%	Qualitative, Yarning	Australia	Study RHD-P health literacy; health services responses.	N/A (none)
8	Bhatla(2003)[56]	TCC-HRPC	n=207 RHD=88%	RC	India	Evaluate CDiP maternal/fetal outcome in developing country.	0%
9	Bhutta(2003)[65]	TCC-HRPC	n=170 RHD=91%	PCS	Pakistan	Determine CDiP outcomes post-cardiac surgery.	0%
10	Chang(2018)[27]	TCC	n=50 n= 25 RHD = 100%	Mixed methods	Uganda	Understand factors/attitudes towards reproductive health & disease in women with RHD.	N/A (none)
11	Chhetri(2014)[35]	TCC-HRPC	n=53 RHD=89%	PCS	Nepal	Investigate prevalence, characteristics, outcomes CDiP.	4%*
12	Chumpathong(2014)[36]	TCC-HRPC	n=175 RHD=66%	RC	Thailand	Evaluate CARPREG predicting cardiac/obstetric/neonatal complications.	3%
13	Curtis(2009)[11]	TCC-HRPC	n=177 RHD=3%	RCS	UK	Describe CDiP; review guidelines adherence, identify suboptimal management.	2%
14	Desai(2000)[49]	TCC-HRPC	n=208 RHD=N/S MS=100%	PCS	South Africa	Evaluate management/outcomes MS in pregnancy.	0%
15	Diao(2011)[5]	TCC-HRPC	n=50 RHD=92%	RCS	Senegal	CDiP maternal/foetal outcomes in a low-income country.	37%*
16	Faiz(2003)[50]	TCC-HRPC	n=126 RHD=N/S MVHD=95%	RCS	Saudi Arabia	Review MVHD during pregnancy: incidence, outcome.	0%

	Study	Setting / Type of care	Study population	Study design	Country(s)	Objectives	Maternal mortality (rounded to nearest percent)
17	Fu(2015)[37]	TCC CDM	n=1086 RHD=15%	RC	China	Identify heart failure risk during pregnancy women with pre-existing disease	1%*
18	Jatavan(2011)[59]	TCC-HRPC	n=125 RHD=49%	RC	Thailand	Determine outcomes CDiP.	0%
19	Kaluarachchi(1995)[66]	TCC-HRPC	n=166 RHD=70%	PCS	Sri Lanka	Evaluate CDiP pattern and outcome.	2%
20	Kanwar(2018)[67]	TCC-HRPC	n=66 RHD=77%	PC	India	Identify feto-maternal CDiP predictors complications/ outcomes ≤28v>28 weeks.	6%
21	Konar(2012)[45]	TCC-HRPC	n=281 RHD=69%	PCS	India	Evaluate CDiP, maternal/perinatal outcome.	1%
22	Kovavisarach(2007)[60]	TCC-HRPC	n=196 RHD=55% (period 3)	RC	Thailand	Assess prevalence, demographics, maternal/perinatal outcomes CDiP (3 study periods).	3%
23	Madazli(2010)[68]	TCC-HRPC	n=144 RHD=87%	RC	Turkey	Evaluate maternal/fetal outcome CDiP developing country.	0%
24	Malhotra(2004)[46]	TCC-HRPC	n=312 RHD=N/S VHD=100%	RC	India	Compare pregnancy outcomes of women with VHD to healthy women.	0.6%
25	Martins(2016)[54]	TCC-HRPC	n=132 RHD=62%	RC	Brazil	Determine CDiP risk factors associated with maternal/neonatal complications.	3%
26	Michaelson-Cohen(2011)[38]	TCC-HRPC	n=175 RHD=41%	PC	Israel	Assess CDiP outcome.	0%
27	Nqayana(2008)[47]	TCC CDM	n=95 RHD=81%	RCS	South Africa	Review CDiP in developing country.	0%
28	Pratibha (2014)[53]	TCC-HRPC	n=200 RHD=100%	RCS	India	Study pregnancy outcomes of RHD-P; evaluate perinatal outcomes of Percutaneous Balloon Mitral Valvuloplasty during pregnancy.	1%*
29	Puri(2013)[39]	TCC-HRPC	n=97 RHD=70%	RC	India	Assess CDiP & associated maternal/fetal complications.	3%
30	Rahman(2000)[61]	TCC-HRPC	n=274 RHD=76%	RCS	Saudi Arabia	Review CDiP outcomes.	0%
31	Rezk(2018)[69]	TCC-HRPC	n=204 RHD=100%	PC	Egypt	Assess cardiac/obstetric outcome in RHD-P & predictors of poor outcome.	0%*
32	Sartain(2012)[58]	TCC-HRPC	n=95 RHD=100%	RC	Australia	Determine maternal-cardiac complications/outcomes in patients with RHD.	0%*
33	Sawhney(2003)[55]	TCC CDM	n=500 RHD=100%	RC	India	Study maternal/perinatal outcomes RHD-P.	2%
34	Schoon(2001)[32]	TCC-HRPC	n=42index+25 referred RHD=33%	RCS	South Africa	Document CDiP mortality/morbidity; compare complicated vs uncomplicated.	18%
35	Schoon(1997)[51]	TCC/regional-HRPC	n=164 RHD=N/S	RCS	South Africa	Describe maternal outcome CDiP.	10%
36	Silversides(2003)[72]	TCC-CDMs x2	n=80 RHD=100%	PC	Canada	Define predictors maternal-cardiac complications in women with MS.	0%*
37	Sliwa(2014)[40]	TCC-CDM	n=225 RHD=25%	PC	South Africa	Investigate spectrum of disease & maternal/fetal outcome in CDM.	4%

	Study	Setting / Type of care	Study population	Study design	Country(s)	Objectives	Maternal mortality (rounded to nearest percent)
38	Soma-Pillay(2008)[41]	TCC-CDM	n=189 RHD=64%	RCS	South Africa	Assess CDiP profile & maternal/fetal outcome, identify risk categories.	3%
39	Stangl(2008)[42]	TCC-HRPC	n=93 RHD=7.5%	RC	Germany	Analyze risks in low/high-risk women with CDiP.	0%*
40	Subbaiah(2013)[70]	TCC-HRPC	n=100 RHD=64%	RC	India	Analyze CDiP & maternal/fetal outcome.	0%*
41	Thanajiraprapa(2010)[71]	TCC-HRPC	n=193 RHD=69%	RCS	Thailand	Identify complications CDiP.	1%
42	Van Hagen(2018)[43]	TCCs. Multiple sites/countries	n=390 RHD=100%	RC	Multiple countries	Assess maternal/fetal outcomes in women with MVHD.	1%*
43	Wasim(2008)[29]	TCC-HRPC	n=160 RHD=N/S	Cross-sectional descriptive	Pakistan	Assess CDiP; feto-maternal outcomes.	4%

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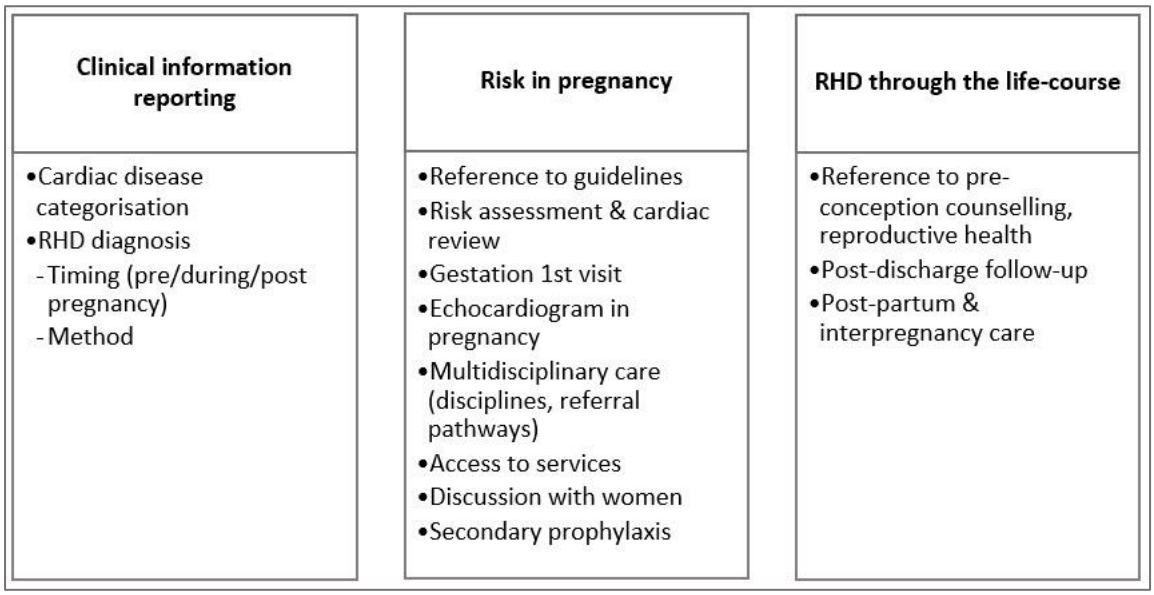
Figure 1: Framework of reporting measures for women with RHD-P



603 **Figure 2: PRISMA diagram of studies with reference to RHD-P**

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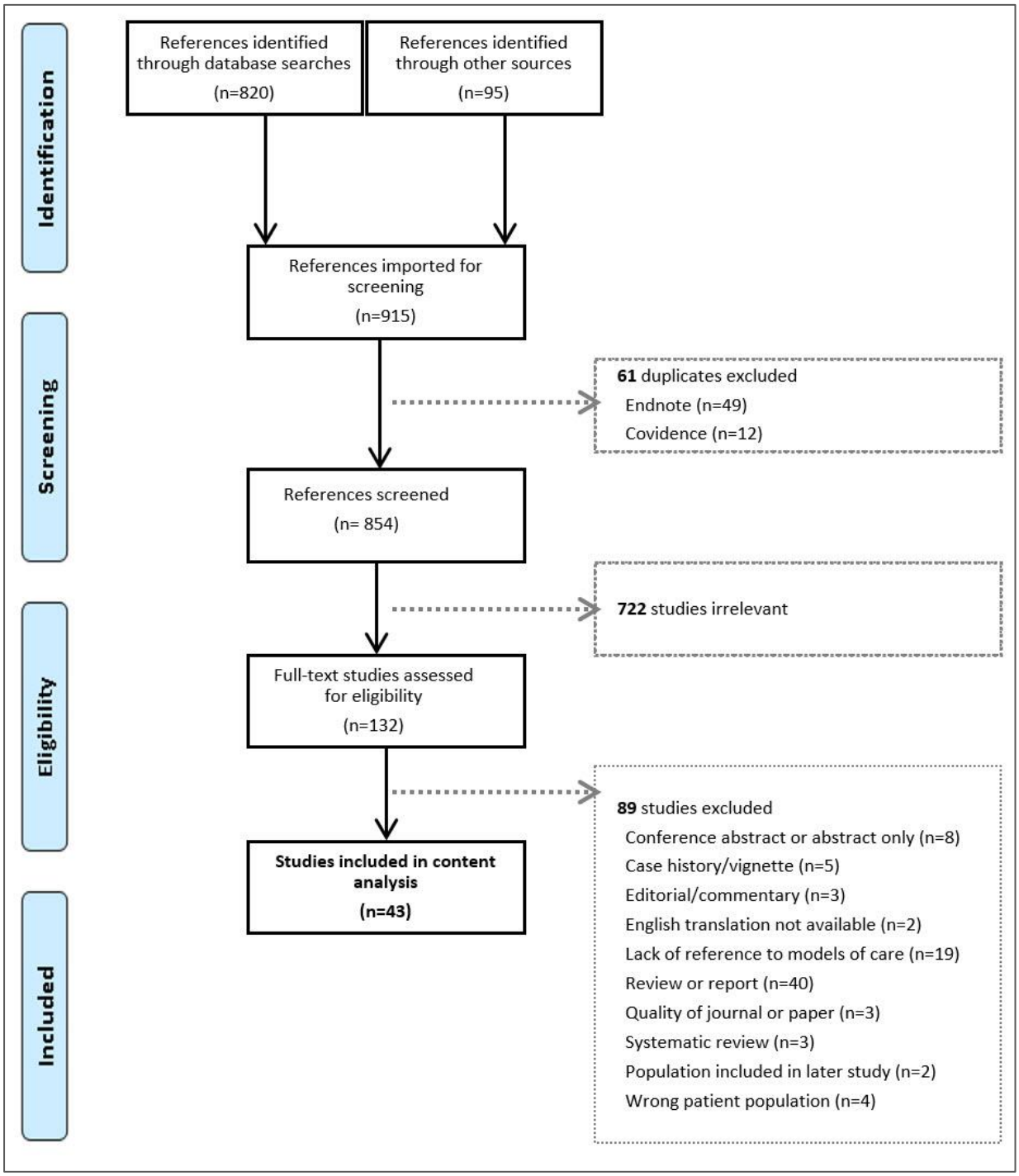

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Figure 3: Number of studies referencing women with RHD-P: by country and World Bank income category

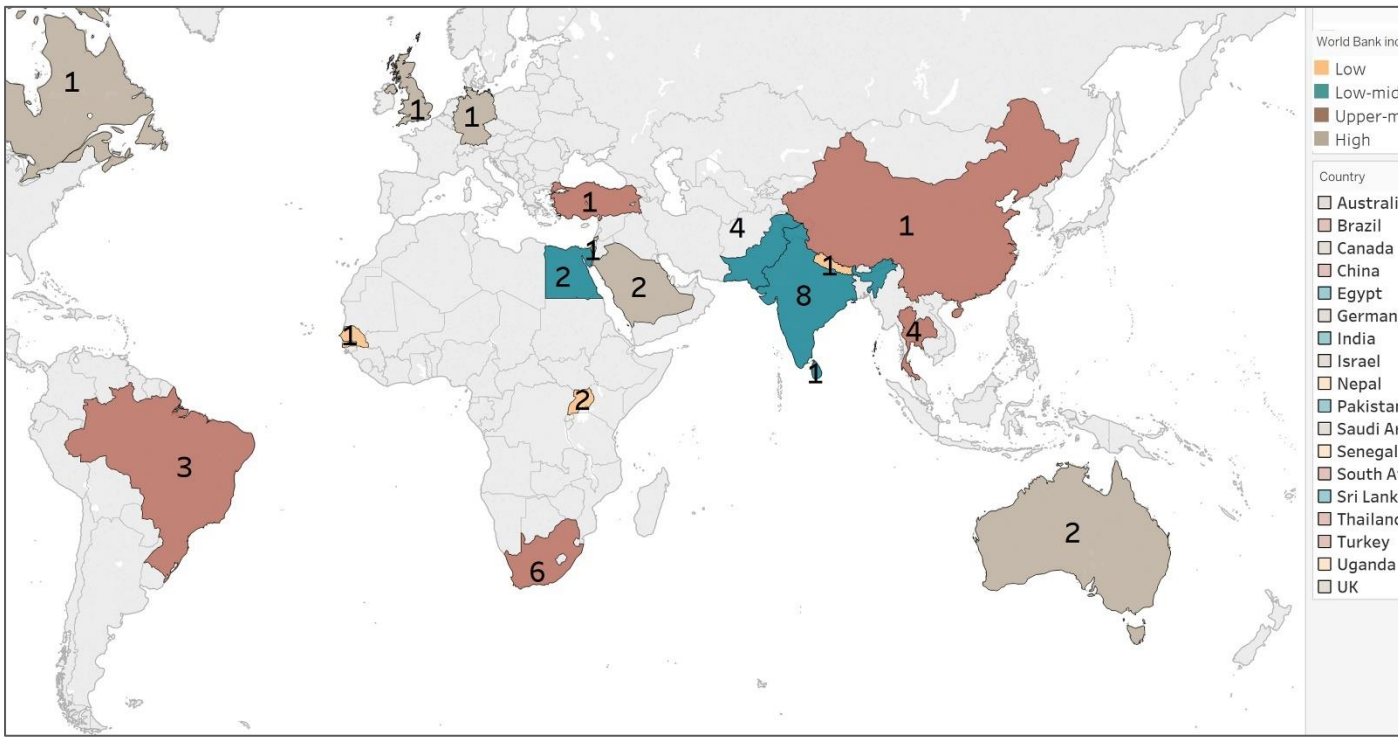

Figure 4: Studies with reference to RHD-P:
core reporting measures and quality appraisal by study

Legend: visual representation of specified reporting measures (outlined in figure 1 framework) according to study. Shaded square indicates the reporting measure was specified in the study; blank square indicates it was not.

Quality appraisal assessed as L (Low), M (Medium), M-H (Medium-high) or H (High).