Medical treatment and anticoagulation in rheumatic mitral stenosis

Septembre 26th 2025

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Competing interests

Consulting and lecture fees from AstraZeneca, Novartis, Boehringer-Ingelheim, Sanofi, Janssen, Bayer, Viatris, Novo-Nordisk

Grants from Pfizer

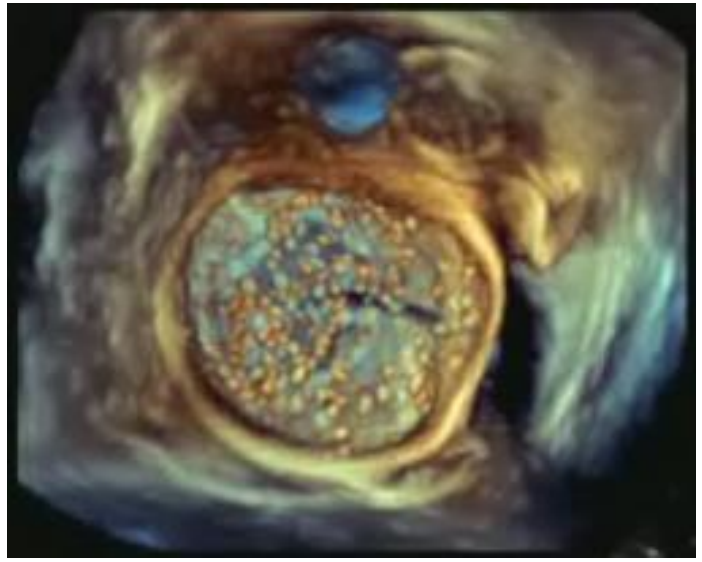
Medical treatment of RHD

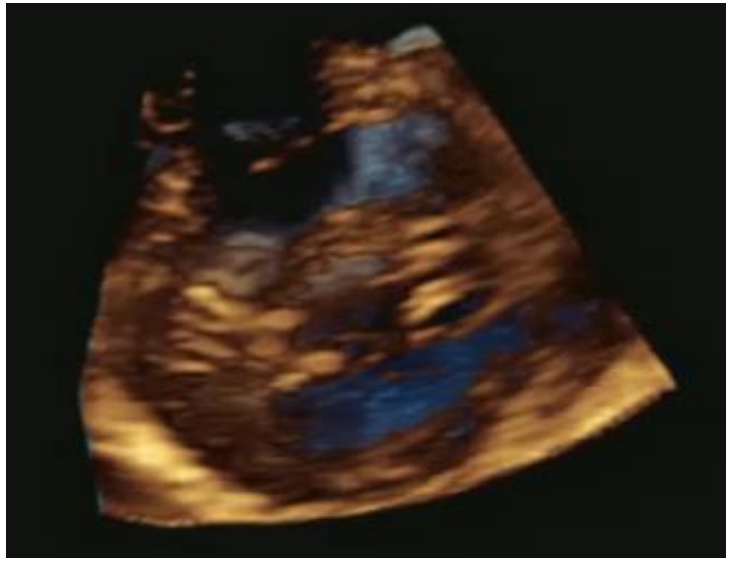
Diuretics, beta-blockers,

± digoxin, non-dihydropyridine calcium channel blockers, ivabradine

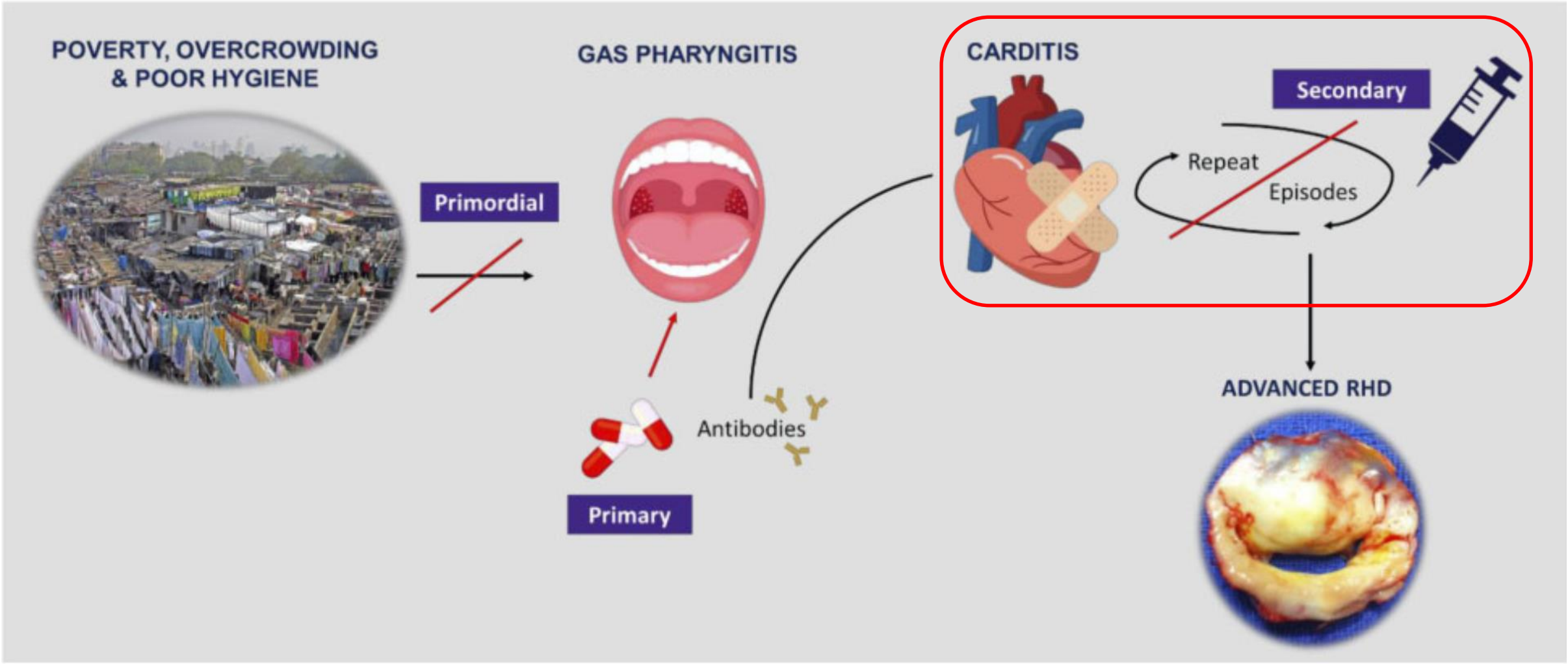
= improve symptoms but no real treatment of MS.

Only interventional treatment for rheumatic MS





Medical treatment of RHD: secondary antibiotic prophylaxis



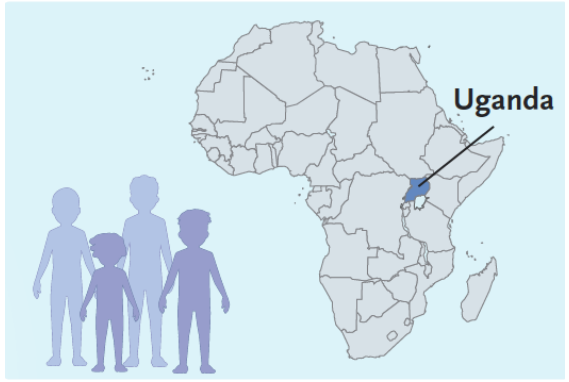
Marijon E et al. European Heart Journal 2021; 42, 3338–3348

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Secondary Antibiotic Prophylaxis for Latent Rheumatic Heart Disease

Randomized, controlled trial in children 5-17 years with latent RHD



SAP vs no treatment

Primary outcome: echocardiographic progression of latent RHD at 2 years

Beaton A, et al. N Engl J Med. 2022;386(3):230-240

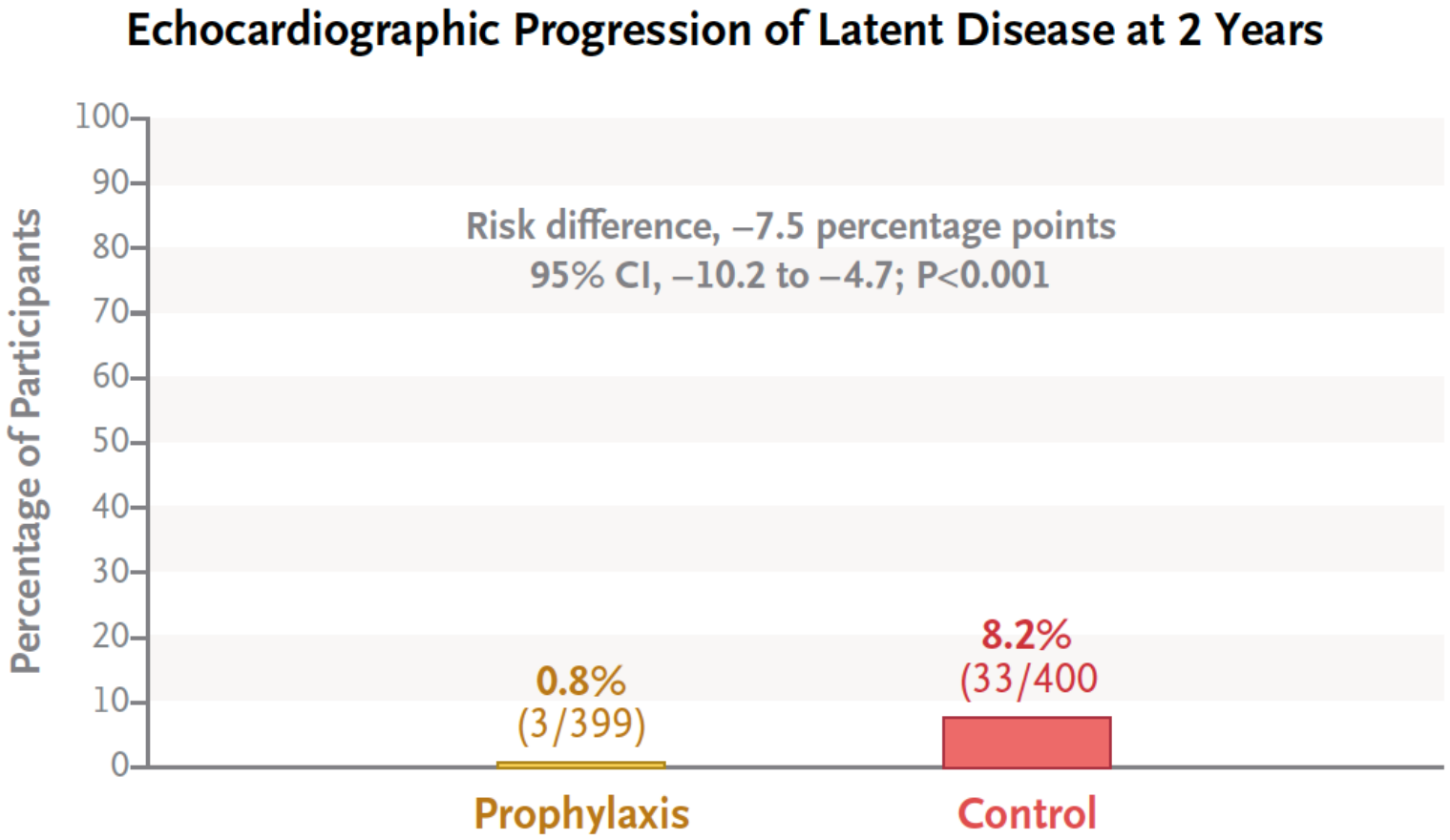
July 2018 - October 2020: 102,200 children screened

Every 4 weeks for 2 years
Administered by trained trial staff

Peer-groups

Community engagement

Outcomes



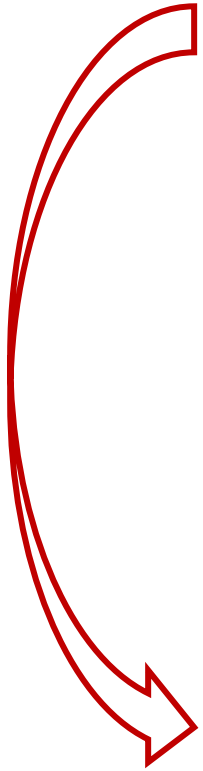
ATB prophylaxis reduced the risk of latent RHD echo progression (P<0.0001)

NNT to prevent 1 child from having progression = **13** (95% CI, 10 to 21)

Beaton A, et al. N Engl J Med. 2022;386(3):230-240

GOAL: far from real-world

- **No transportation costs**
- **Financial incentive, drinks/snacks**



- Monthly RHD peer support group
- Home visits

Adherence to treatment

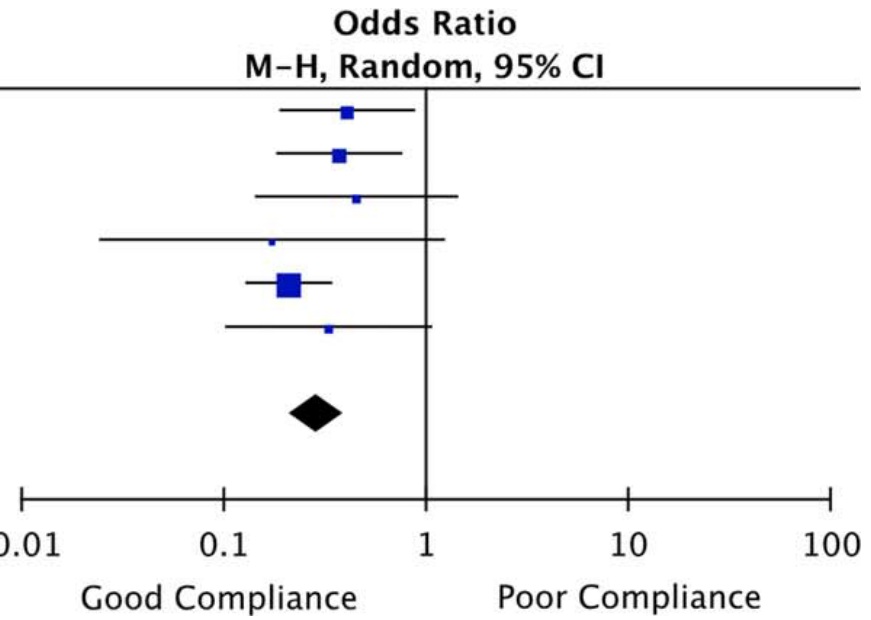
At 2 years,
Monthly injection: **99.1%**

Effective SAP needs good adherence to penicillin

Study or Subgroup	Good Compliance Events	Good Compliance Total	Poor Compliance Events	Poor Compliance Total	Weight	Odds Ratio M-H, Random, 95% CI
Bassili, et. al., 2000	23	82	22	45	17.6%	0.41 [0.19, 0.87]
Belay et. al, 2022	40	228	16	44	20.5%	0.37 [0.18, 0.75]
de Dassel et. al., 2018	5	15	53	101	7.7%	0.45 [0.14, 1.42]
Haran et. al., 2018	3	16	4	7	2.6%	0.17 [0.02, 1.22]
Pelajo et. al., 2010	40	398	48	138	44.1%	0.21 [0.13, 0.34]
Taddio, et. al., 2020	6	215	6	75	7.5%	0.33 [0.10, 1.06]
Total (95% CI)		**954**		**410**	**100.0%**	**0.29 [0.21, 0.40]**
Total events	117		149			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.94$, df = 5 (P = 0.56); $I^2 = 0\%$

Test for overall effect: Z = 7.64 (P < 0.00001)



Good adherence to penicillin reduced ARF recurrence/RHD progression by 71% (p <0.0001)

de Dassel JL, et al. J Am Heart Assoc 2018;7:e010223
Ambari AM, et al. Ann Med Surg. 2024;86(4):2116-2123

Barriers to SAP: poor adherence to IM penicillin

Patient and family barriers :

- pain and fear of injections
- missed work/school
- long distance to clinics
- highout-of-pocket travel costs
- long waiting time for injections

Health system-level barriers:

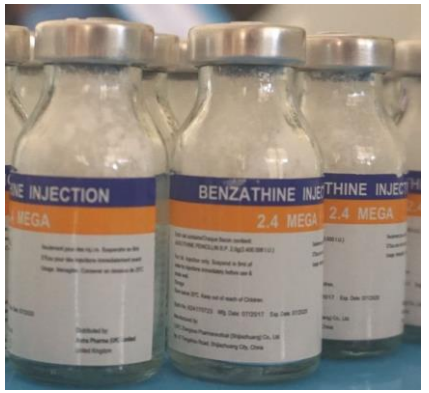
- unskilled providers for injections

Use of oral penicillin prophylaxis ?

Rwebember J, et al. Am Heart J 2024;275:74–85
Huck DM , et al . Glob Heart 2015;10:63–9 e1
Musoke C , et al . Cardiovasc J of Afr 2013;24:124–9
Longenecker CT , et al . Circulation 2017;10:e004037
Ndagire E , et al . PLoS Negl Trop Dis 2021;15:e0009164

RRCU
RHD RESEARCH COLLABORATIVE IN UGANDA

Intramuscular versus enteral penicillin prophylaxis to prevent progression of rheumatic heart disease: Study protocol for a noninferiority randomized trial (the GOALIE trial)



1. Compare the proportion of children aged 5-17 years with latent RHD receiving oral penicillin who progress to worse valvular disease at two years compared to children who receive intramuscular (IM) penicillin.
2. Evaluate the economic equivalence and cost-effectiveness of oral penicillin compared to IM penicillin, after echocardiographic screening for latent RHD detection.
3. Compare patient-reported and parent-reported outcomes (treatment acceptance, treatment satisfaction, and health-related quality of life) between children receiving oral and IM penicillin prophylaxis.

Rwebember J, et al. Am Heart J 2024;275:74–85

Long-term SAP with injectable penicillin

Patients with established RHD: long-term SAP with Injectable benzathine penicillin G 1.2 million (IU) every 3–4 weeks over 10 years is recommended to prevent recurrent episodes.

Long-term prophylaxis into adulthood should be considered in high-risk patients according to the severity of VHD and exposure to group A Streptococcus.

Praz F et al. EHJ 2025; 00,1-102
Sanyahumbi A, et al. J Am Heart Assoc. 2022;11(5):e024517
Kumar RK, et al. Circulation 2020;142:e337–57.
WHO Guideline. https://www.who.int/publications/i/item/9789240100077

Anticoagulation in MS

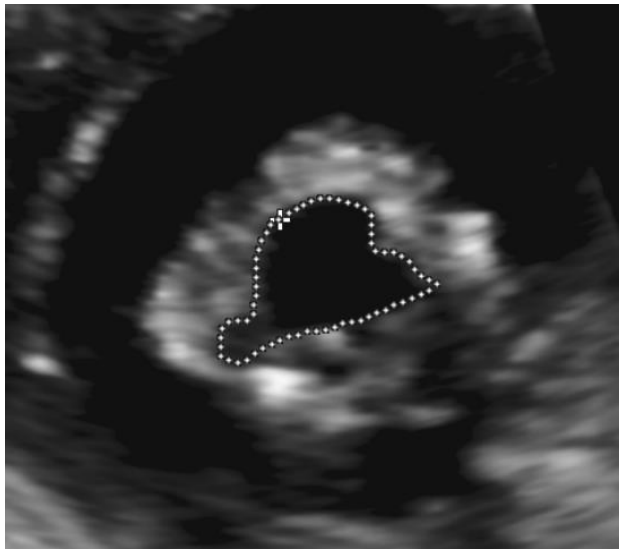
- Sinus rhythm

OAC after systemic embolism or LA thrombus

dense spontaneous echocardiographic contrast or enlarged LA (diameter >50 mm or volume >60 mL/m2)

- Afib ++

Prevalence of AF in RHD = 39%

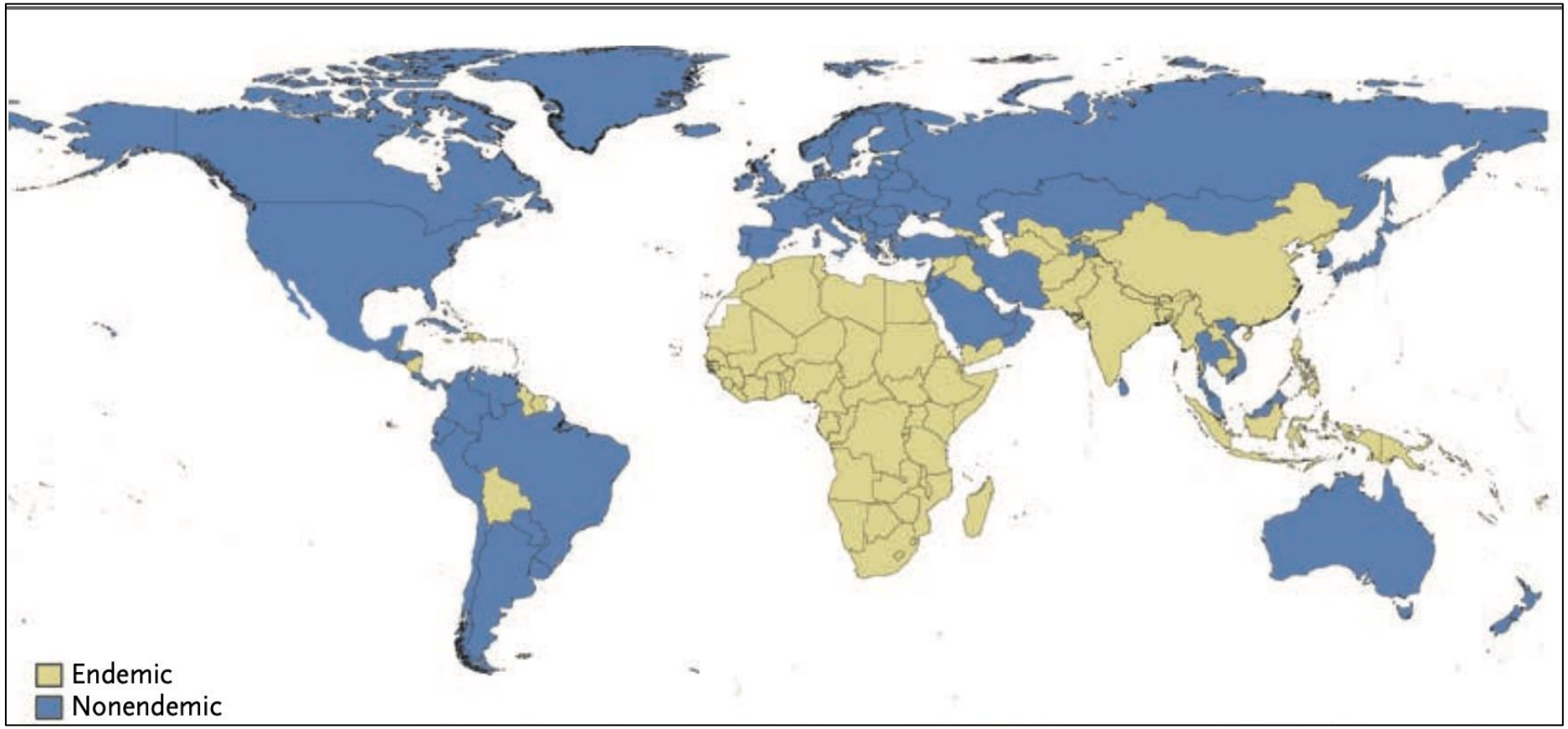


Keenan NG, et al. Am J Cardiol 2010;106:1152–6.
Praz F et al. Eur Heart J 2025; 00,1-102
Diker E, et al. Am J Cardiol. 1996;77:96-8

Burden of RHD in LMIC

33.4 million cases worldwide

RHD: the most common manifestation of VHD worldwide



Largest numbers of cases :

- India (13.17 million cases)
- China (7.07 million)
- Pakistan (2.25 million)
- Indonesia (1.18 million)

Watkins D, et al. NEJM 2017; 377:713-22

Poor quality of VKA anticoagulation in LMIC

- lower prescription of VKA ⟹

- China: 11% of patients with AF and CHA2DS2VASc score≥ 2
- India: 40%
- **Western Europe: 63%.**

Ramakumar V, et al. Indian Heart J. 2021;73:244-248
Bai Y, et al. Chest. 2017;152: 810-20

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- lower proportion of INR values in the therapeutic range ⟹

  India & China: TTR 35 and 36%

  Rural India: 13%

  Western Europe: 67%

Acceptable TTR > 60%
Optimal TTR > 70%

Ramakumar V, et al. Indian Heart J. 2021;73:244-248
Bai Y, et al. Chest. 2017;152: 810-20
Oldgren J, et al. Circulation 2014 ;129:1568-76
Connolly SJ, et al. Circulation. 2008;118:2029-37

Poor quality of VKA anticoagulation in LMIC

- Lack of patient awareness
- Fewer facilities for and poor access to INR testing and VKA management
- Cost of INR tests and physician consultation for dose adjustment

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⇨ **NOACs to improve anticoagulation quality ?**

Ramakumar V, et al. Indian Heart J.;73:244-248
Bai Y, et al. Chest. 2017;152: 810-20
Oldgren J, et al. Circulation 2014 ;129:1568-76
Chebrolu P, et al. Indian J Med Res. 2020;152:303-307

Anti-IIa and Anti-Xa vs. VKA in AFib

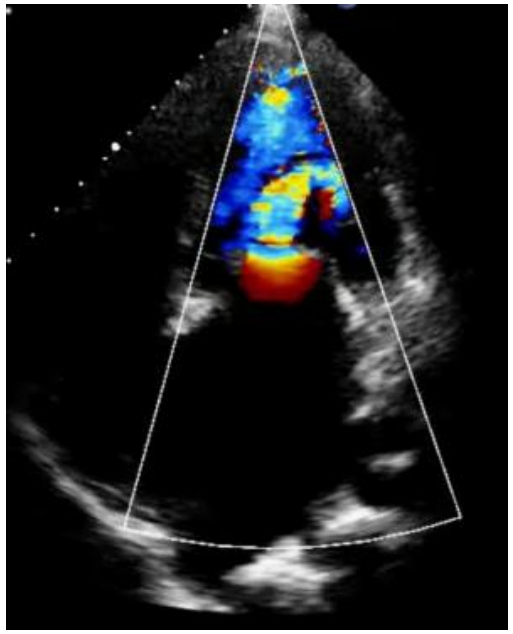
Exclusion of pts with  **« valvular AF »** 

	Rely (Dabigatran)	Rocket AF (Rivaroxaban)	Aristotle (Apixaban)	Engage AF (Edoxaban)
n=	18 113	14 264	18 201	21 105
Mean age	72	73	70	72
$CHADS_2$	2.2±1.2	3.5±0.9	2.1±2.1	2.8±1.0
Contra-indications	**Relevant valve disease and prostheses**	**Mitral stenosis, prostheses**	**Mitral stenosis, prostheses**	**Mitral stenosis, mechanical prostheses**
	79% MR, 21% AR, 3% AS, 5% mild MS	90% MR, 25% AR, 1.5% AS, <5% had RHD	73% MR, 18% AR, 2% AS, 2.7% mild MS	80% MR, 13% AR, 1% AS

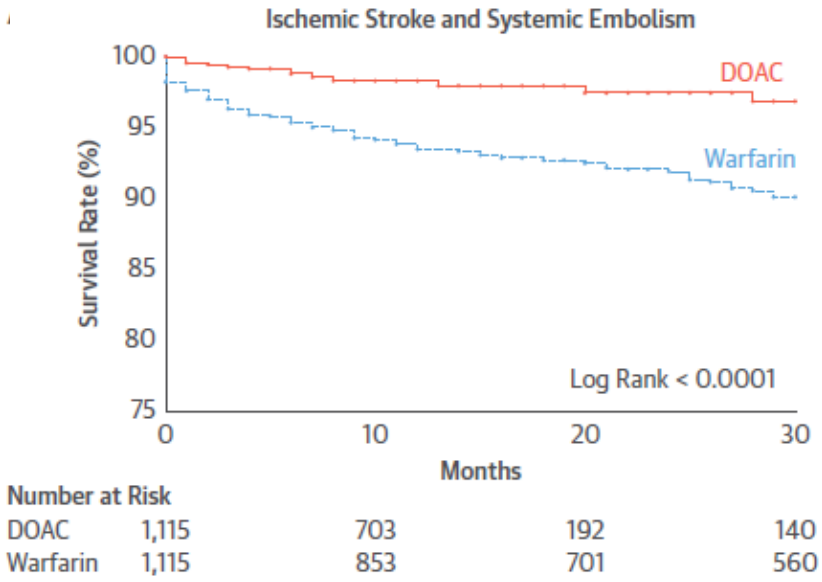
Connolly SJ, et al. N Engl J Med 2009;361:1139-51
Patel MR, et al. N Engl J Med 2011;365:883-91
Granger CB, et al. N Engl J Med 2011;365:981-92
Guigliano RP, et al. N Engl J Med 2013;369:2093-104

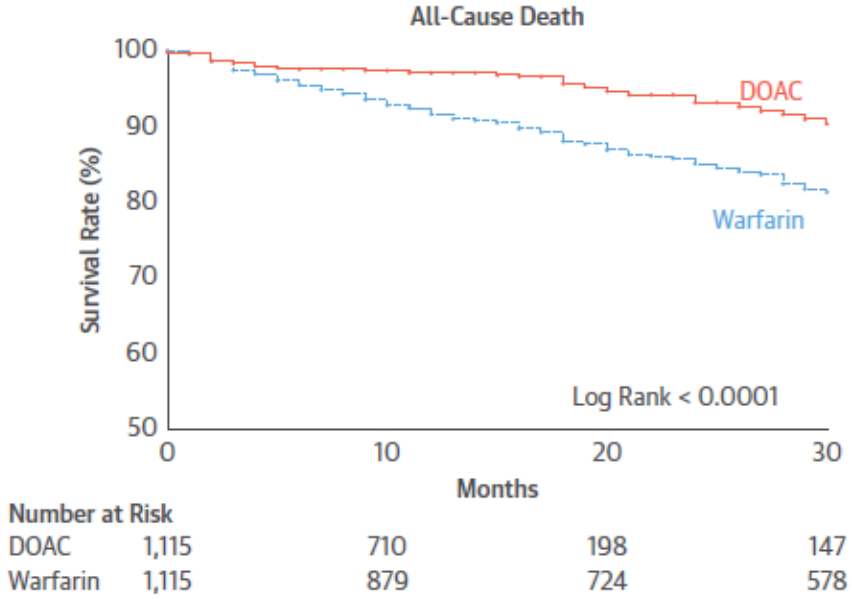
Initial hope regarding NOACs and Afib in MS

Observational study with large groups and propensity score matching, any degree of MS



- 1115 pts under VKA (Warfarine)
- 1115 pts with NOACs





Kim JY, et al. J Am Coll Cardiol 2019;73:1123-31

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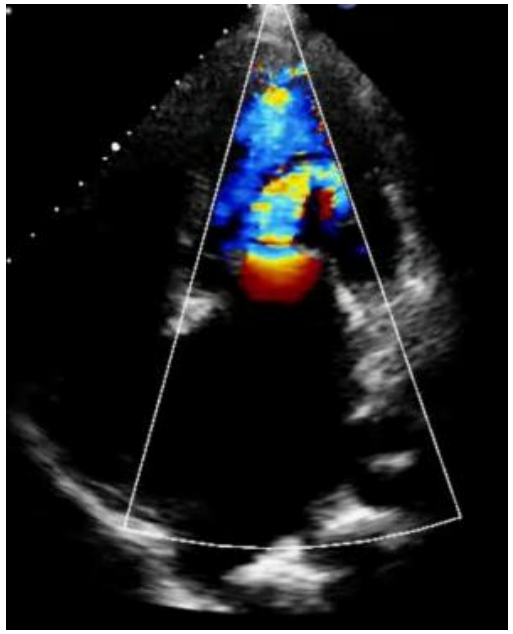

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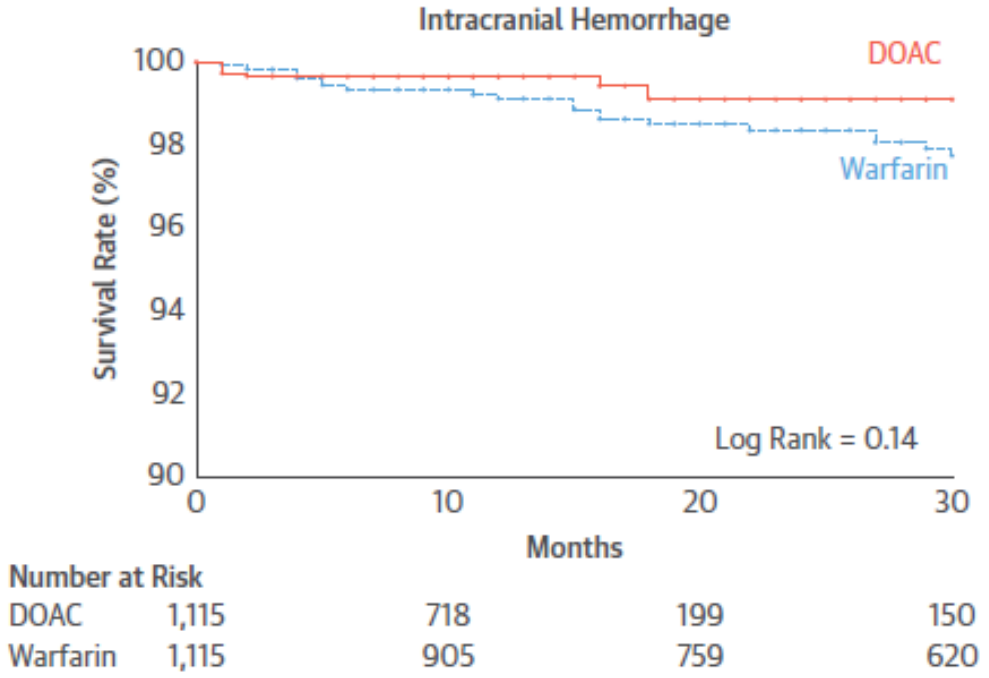

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The NEW ENGLAND JOURNAL of MEDICINE

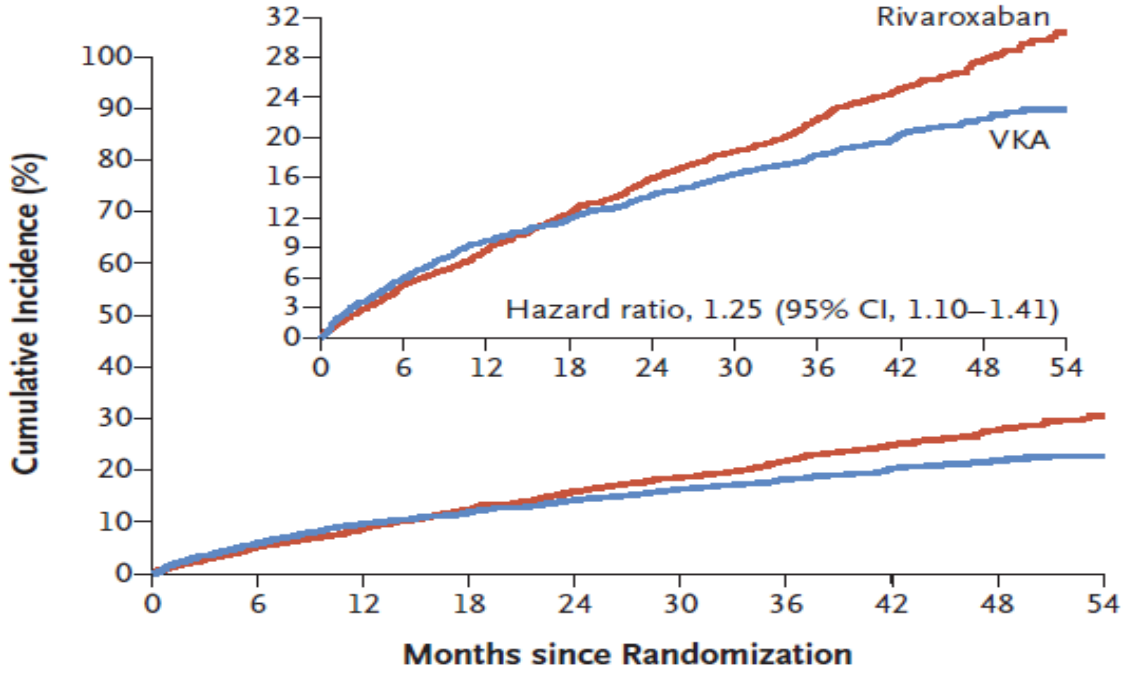
ORIGINAL ARTICLE

Rivaroxaban in Rheumatic Heart Disease–Associated Atrial Fibrillation

4531 pts, 82% of MS (66% severe)
Mean age 50 years, 72% female
Randomized between Rivaroxaban or VKA

Superiority of VKA for:

- Major composite criterion of stroke/SEE, MI, CV death
- All-cause death



Connolly, et al. N Engl J Med 2022;387:978-88

INVICTUS: a matter of debate

Open-label trial

VKA :monthly INR monitoring
No FU for rivaroxaban group

improved medical care in the VKA arm

VKA reduced the risk of CV death or morbidity by 25%, without increasing major bleeding, compared to rivaroxaban

Dougherty S, et al. Eur Heart J 2023;44:2440–2442

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Algorythm for INR adjustment

No intuitive dose monitoring
(usual practice)

TTR 32% before inclusion
59% at 1 year FU
64% at 4 year FU

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Adherence to treatment

- At 1 year,

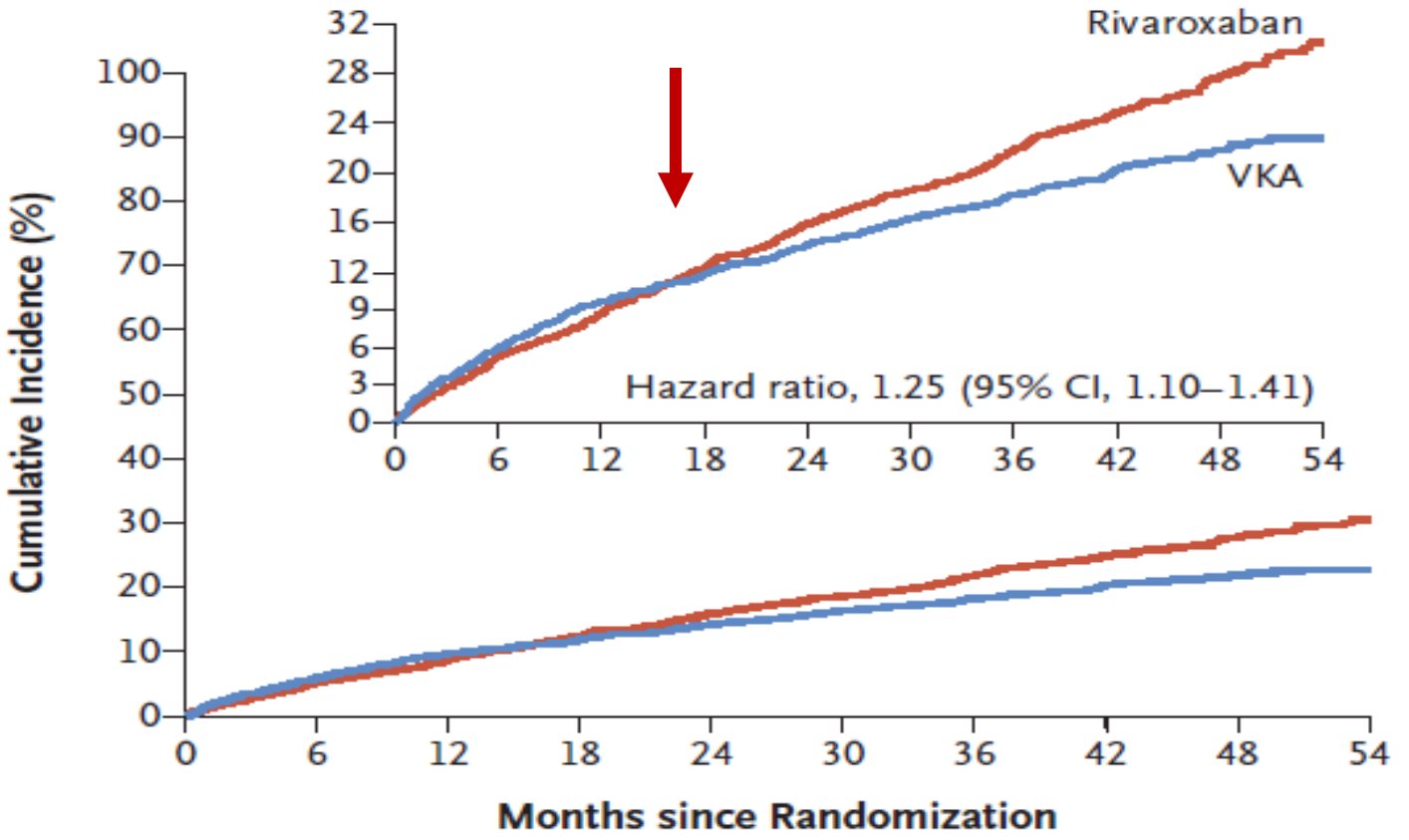
Rivaroxaban 89% vs. VKA 98%

- At 4 years,

Rivaroxaban 79% vs. VKA 96%

Dougherty S, et al. Eur Heart J 2023;44:2440–2442

INVICTUS: a matter of debate

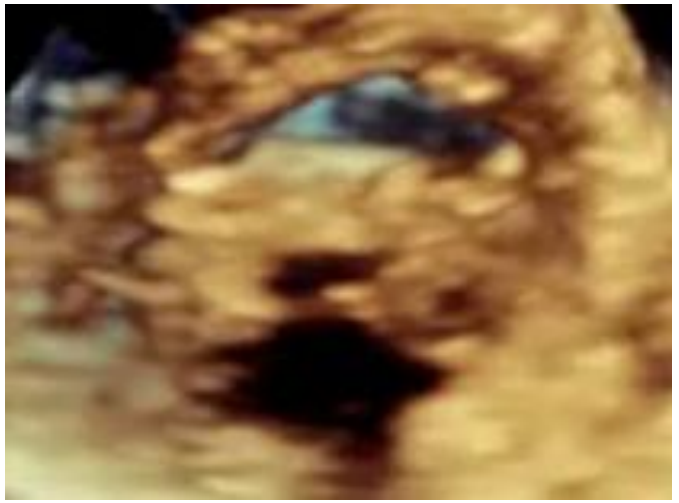


No. at Risk										
Rivaroxaban	2275	2124	2023	1931	1838	1750	1356	876	451	144
VKA	2256	2100	2003	1944	1880	1809	1392	881	462	138

Connolly SJ, et al. N Engl J Med 2022;387:978-88

NOACs are contra-indicated in case of MS

Recommendations	Class	Level
The use of DOACs is not recommended in patients with AF and rheumatic MS with an MVA ≤2.0 cm^2.[165]	III	B



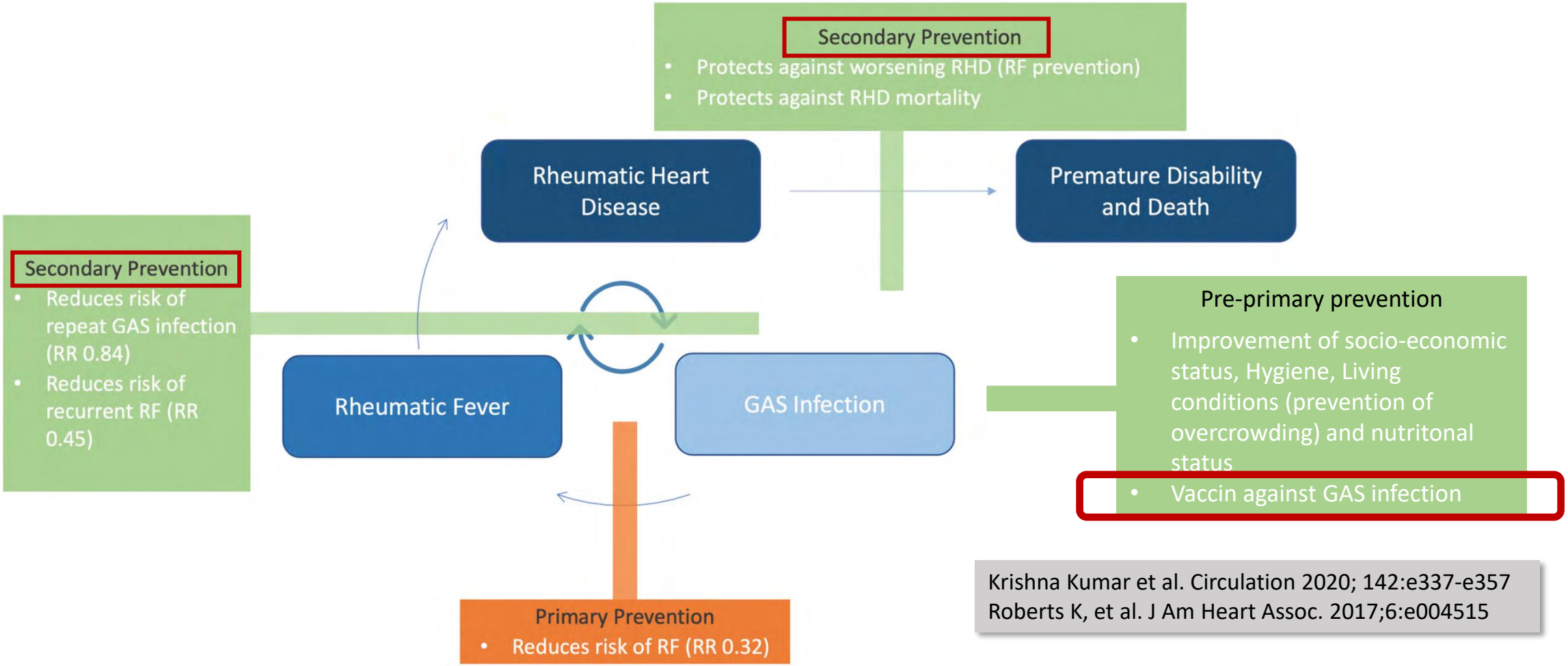
Praz A, et al. Eur Heart J. 2025;00:1-102

Take-home messages

- BB-, diuretics…: only symptomatic treatment. No medical treatment of severe MS, only intervention (PMC or surgery)
- Anticoagulation with VKA if MS $\leq$ 2 cm^2
- Secondary antibiotic prophylaxis: needed and effective. Hopes regarding oral penicillin

Medical treatment of rheumatic MS

Echo screening and early initiation of SAP : cost-effective strategy for RHD management



Krishna Kumar et al. Circulation 2020; 142:e337-e357
Roberts K, et al. J Am Heart Assoc. 2017;6:e004515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LIÈGE
SEPTEMBER
25&26 2025

Thank you !